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Epidural and Spinal Analgesia and Anesthesia: Contemporary Issues

M. S. BATRA, MD, GUEST EDITOR

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M.S. Batra

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J.A.W. Wildsmith

The great attraction of spinal (subarachnoid) anesthesia is that very profound block to nerve conduction can be produced over large areas of the body with very small amounts of drug. The great challenge in clinical practice is to control the spread of that drug through the cerebrospinal fluid so that the extent of block is adequate for the projected surgery, but not so widespread that the risk of complications is unnecesarily great. This article reviews the history of spinal anesthesia, correct drugs and their administration, and factors affecting duration.

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Michael F. Mulroy

Epidural anesthesia carries the risk of unintentional intravascular injection of toxic doses of local anesthetic. The use of a 15-μg epinephrine test dose will indicate intravascular injection by producing a 20-beats per minute increase in the heart rate of normal subjects within 60 seconds. In patients receiving beta blockers, this tachycardia is abolished, and systolic blood pressure must be monitored. In the pregnant patient in labor, this test is ineffective, and incremental injection of small quantities of drug are used to avoid toxicity. Elderly patients may also have reduced sensitivity to this test. Over all, however, the epinephrine test dose remains the most reliable defense against unintentional intravascular injection.

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Epidural analgesia benefits both mother and fetus and is the only effective way to treat labor pain. Contemporary practice emphasizes excellent sensory analgesia with minimal motor block and the concept of "ambulatory pain relief." Recent developments in epiduroscopy and nuclear magnetic resonance imaging add to our knowledge of epidural space anatomy, confirm the existence of a dorsomedian "band," and suggest technical advantages for the paramedian approach. Continuous infusion epidural analgesia studies suggest that the technique gives comparable or improved pain relief, but at the price of increased motor block and more local anesthetic. New techniques include patient-controlled epidural analgesia. Epidural analgesia has a good safety record and few complications, although episodes of unsatisfactory block, postpartum backache, and postdural puncture headache underline the need for preventive care and early management of complications.

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Joseph M. Neal

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J. David Haddox

The treatment of pain by instillation of steroids into the epidural space has been done for decades. Few well-designed, unbiased studies have been done. This article examines the extant data and opinions regarding possible mechanisms of action and the therapeutic role. Further studies are necessary to prove or to disprove efficacy or, more importantly, to define the appropriate indications for this therapy.

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EPIDURAL AND SPINAL ANALGESIA AND ANESTHESIA: CONTEMPORARY ISSUES

FOREWORD

The last few years have witnessed a dramatic renewal of interest in regional anesthesia, and there have been four primary reasons for this renewed interest. First, new equipment, techniques, and drugs have greatly increased the capabilities of regional anesthesia. Second, new operations and procedures have greatly increased the applications of regional anesthesia. Third, the explosion of interest in and enthusiastic acceptance of intensive pain management in the postoperative period by our surgical and medical colleagues have greatly expanded the role of the anesthesiologist and regional anesthesia in these areas. Fourth, epidural and spinal anesthesia and analgesia, although improving patient comfort in the postoperative period, have also been shown to decrease surgical morbidity; consequently, the patient who has had regional anesthesia may require less intensive and expensive postoperative care and spend fewer days in the hospital. Thus, the topic of this issue of *Anesthesiology Clinics of North America*, "Epidural and Spinal Analgesia and Anesthesia: Contemporary Issues," is an extremely important and timely one, and it explores in depth the concepts and practical details that enhance efficacy, reduce morbidity, and increase patient satisfaction while allowing use of regional anesthesia in situations that were considered unlikely in the past.

Dr. M. S. Batra is extremely well qualified to guest edit this issue on regional anesthesia. He has been practicing, researching, and teaching regional anesthesia for over two decades, and his everyday practice leaves no doubt that well-done regional anesthesia is not only pain free but is safe, is cost and time efficient, and results in great patient satisfaction. As a consequence of his outstanding expertise and other highly significant contributions to the practice of regional anesthesia, he has been recognized at the national and international level. He is very actively involved in the activities of several organizations that teach and promote the practice and investigation in the field of regional anesthesia for surgery, obstetric cases, and pain management. In the past, Dr. Batra has been Director of outpatient clinics as well as obstetric anesthesia services. Finally, he has extensive experience in organizing several major nationally prominent postgraduate education programs. In summary, this issue of *Anesthesiology Clinics of North America* is a compelling issue to read for all anesthesiologists. The timeliness and importance of the subject matter and the expertise of the guest editor ensures that the issue will contain high-quality and exciting concepts and clinically relevant and valuable practical instruction.

JONATHAN L. BENUMOF, MD
Consulting Editor

FORTHCOMING ISSUES

June 1992

CURRENT CONCEPTS IN ACUTE PAIN CONTROL
Alan N. Sandler, MD, *Guest Editor*

The safe control of acute perioperative pain is most often the treating physician's highest priority. Consequently, it is no surprise that research into acute pain control and useful developments stemming from this research have occurred at an extremely rapid pace. The rapid pace of important developments in acute pain control requires that reviews of clinically relevant progress appear every few years to best enable the practicing anesthesiologist to control acute pain. This issue of *Anesthesiology Clinics of North America* covers the entire breadth of important intellectual and practical considerations in acute pain control. The issue is guest edited by Dr. Alan Sandler, who is internationally recognized for his clinical, research, and teaching contributions. Dr. Sandler's extensive academic and intellectual credentials and expertise guarantee the quality of the issue.

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Vladimir Kvetan, MD and T. James Gallagher, MD,
Guest Editors

EPIDURAL AND SPINAL ANALGESIA AND ANESTHESIA: CONTEMPORARY ISSUES

PREFACE

The use of neuraxial blockade, which includes epidural and spinal anesthesia and the modulation of spinal neural transmission to produce selective analgesia, has grown explosively in the last decade and a half. The development of newer local anesthetics with unique characteristics and a better understanding of properties of older agents has caused a resurgence in the use of regional anesthesia. The discovery of opioid receptors in the spinal cord and the development of highly lipophilic narcotics has helped to transform the area of acute and chronic pain management. This has been coupled with phenomenal advances made in the delivery systems used to administer drugs into the epidural and subarachnoid space. These developments have not been limited to the perioperative period or the management of postoperative and chronic pain. Pain relief during childbirth and management of complicated obstetrics has become safer. Selective analgesia without unwanted sensory and motor block during labor and the ability to intensify analgesia and to provide anesthesia rapidly for unanticipated obstetric interventions is beginning to make the use of neuraxial blockade most desirable, both to the parturient and to the obstetrician. Advances have also been made in better understanding the toxic effects and complications of local anesthetics and regional block techniques. Considerable activity in the area of prevention of side effects and complications has been very fruitful, which is allowing us to use neuraxial blockade much more safely and in many more situations.

This issue on contemporary developments in neuraxial blockade is not only timely but also necessary to provide useful and practical guidelines that can be used by most anesthesiologists. An effort has been made to include topics that explore concepts and suggest ways to improve patient care. Some areas may appear brief as it is impossible to be expansive in an issue of this nature, but a sincere effort has been made to examine areas that are most critical. Its the little things we do in medicine that sometimes make the biggest impact on patient outcome and satisfaction.

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ANTICOAGULANTS, ANTIPLATELET THERAPY, AND NEURAXIS BLOCKADE

Terese T. Horlocker, MD, and Denise J. Wedel, MD

Spinal and epidural blockade are frequently used for intraoperative anesthesia and postoperative analgesia for orthopedic and vascular procedures. The theoretical advantages of regional over general anesthesia in these patients include decreased incidences of cardiopulmonary complications and deep venous thrombosis, as well as the benefits of postoperative analgesia.[13, 19] In addition, patients undergoing vascular surgery benefit from the associated sympathetic blockade and enhanced blood flow to the lower extremities.[2] However, many of these patients receive anticoagulation or thrombolytic therapy preoperatively for thrombolic prophylaxis and are not considered candidates for regional anesthesia because of a theoretically greater risk of hemorrhagic complications. The actual risk of such complications is difficult to define accurately and must be weighed against the potential benefits gained.

Neurologic dysfunction after bleeding into the spinal canal is a rare complication of spinal and epidural anesthesia. Hemorrhage and hematoma formation may occur (1) spontaneously, (2) in association with anticoagulation or antiplatelet therapy, (3) due to preexisting vascular abnormalities, (4) in association with neoplastic disease, and (5) due to trauma to vascular structures by the introduction of a needle into the subarachnoid or epidural space. The actual incidence of such complications associated with spinal or epidural anesthesia is unknown;

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however, the incidence of paraplegia cited in the literature is less than 1 in 10,000 procedures.[7] With such an infrequently occurring event, in order to define and reduce the risk of serious hemorrhagic complications, it is necessary to be familiar with not only the clinical studies of patients undergoing spinal or epidural anesthesia while receiving anticoagulants, but also the pharmacologic parameters of the anticoagulant and antiplatelet agents themselves.

ANTICOAGULANTS

Spinal hematomas can occur spontaneously following anticoagulation therapy, without obvious trauma or needle placement. Over 100 spontaneous epidural hematomas have been reported, 25% of which are associated with anticoagulation therapy.[29] Of the 34 reported spinal hematomas occurring after lumbar puncture, 14 (41%) were associated with anticoagulant therapy.[22] Only two of the patients were given anticoagulants before lumbar puncture.

Patients hospitalized for major vascular and orthopedic procedures frequently have anticoagulation therapy perioperatively to prevent thrombosis and embolism. Many of these patients are administered minidose heparin or warfarin preoperatively.[20] The decision to perform regional anesthesia on these patients must be made on an individual basis, with the proper evaluation of indications and contraindications. Understanding the mechanisms of blood coagulation and pharmacologic properties of these drugs is essential to this decision-making process.

INDIRECT ANTICOAGULANTS

Oral anticoagulants are occasionally initiated before major joint surgery in anticipation of continuing these agents during the postoperative period. Vitamin K antagonist drugs, such as warfarin or dicumarol, exert their anticoagulant effect by blocking a structured modification of the vitamin K–related coagulation factors (II, VII, IX, X). Patients show varying sensitivities to indirect anticoagulants. Sensitivity to drugs of the coumarin series was normal in 60% of patients, increased in 20%, while the remaining 20% showed resistance.[17] Unlike heparin, the anticoagulant effect of these drugs is not immediate, but is dependent on the reduction of the level of vitamin K–dependent clotting factors. Since factor VII has a relatively short half-life (6–8 hours), the prothrombin time will be prolonged into the therapeutic range (1.5–2 times normal) in 24 to 36 hours. However, an adequate level of anticoagulation is not achieved until factor II and X activity is sufficiently depressed, requiring 4 to 6 days.[12] Even with high loading doses of warfarin (15–20 mg), anticoagulation is not therapeutic for 48 to 72 hours.[14] Similarly, the anticoagulant effects persist for 4 to 6 days after therapy is terminated while new vitamin K coagulation factors are synthesized. In an emergent situation, the anticoagulant effects can be reversed by transfusing fresh frozen plasma.

DIRECT ANTICOAGULANTS

Heparin is a complex polysaccharide that exerts an anticoagulant effect by accelerating the inhibition of activated coagulation factors by antithrombin III. There are at least six activated clotting factors that can be inhibited by antithrombin III (thrombin, factors XIIa, XIa, IXa, Xa, and kallikrein; Fig. 1).[12]

Patients react with different sensitivities to heparin, making it impossible to predict an individual's response. Highly sensitive patients exhibit a greater increase in the coagulation time and prolonged effect with an intravenous or subcutaneous injection compared with patients with normal or low sensitivity. A number of factors affect an individual's sensitivity including diet, cardiac status, liver disease, and general medical condition.[17]

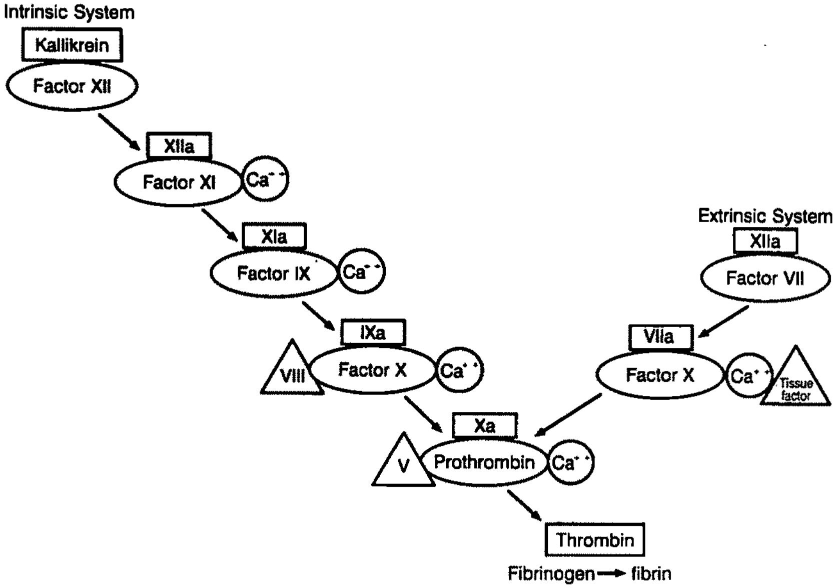

Figure 1. Schematic of the clotting mechanism. The blood coagulation system can be visualized as a cascade of distinct reaction stages in which a precursor protein is converted from its inactive circulating form into an active form. Traditionally, the clotting system consists of two pathways—the intrinsic system, which involves components normally formed in the circulation, and the extrinsic system, which uses a tissue factor in addition to blood components. Heparin enhancement of antithrombin III inactivation occurs with all components (enclosed in rectangles) except factor VII. Vitamin K–antagonist drugs will effect factors VII, IX, X, and prothrombin.

Five minutes after intravenous injection of 10,000 U of heparin, coagulation time is prolonged three to four times. Heparin has a relatively short half-life in circulating blood, 1½ to 2 hours.[12] Four to 6 hours after the administration of a therapeutic dose of heparin, its effect ceases. Following intramuscular or subcutaneous injection of 5000 U, the anticoagulation effect is observed in 40 to 50 minutes and usually returns to baseline in 4 to 6 hours.[17] Often the activated thromboplastin time is not monitored in patients on low-dose heparin, so the coagulation status of these patients is unknown.

ANTICOAGULANTS AND CENTRAL NEURAXIAL BLOCKADE

Quantification of the increased risk of preoperative coumadin therapy for patients receiving central neural blocks is difficult to determine. Odoom and Sih[21] performed 1000 continuous epidural anesthetics in 950 patients undergoing vascular procedures who were receiving oral anticoagulants preoperatively. The thrombotest (a test measuring factor IX activity) was decreased and the partial thromboplastin time was prolonged in all patients before epidural puncture. They excluded from their study patients with blood dyscrasias, prior heparinization, aspirin therapy of long duration, or a thrombotest below 10%. Heparin was administered intraoperatively at a rate of 250 to 300 μg heparin per minute. The epidural catheters were removed 48 hours postoperatively. There was no mention of coagulation status at the time of catheter removal. None of the patients developed any neurologic complications. The authors concluded that provided adequate precautions are taken, epidural analgesia can be safely performed in patients receiving anticoagulant therapy. Rao and El-Etr[26] reported 3164 patients who had continuous epidural anesthesia and 847 who had continuous spinal anesthesia for lower extremity vascular procedures. None of the patients received anticoagulation therapy preoperatively. Intraoperatively, patients were anticoagulated 1 hour after initiating the regional anesthetic, with incremental doses of heparin to maintain their activated clotting time twice the baseline value. Twenty-four hours after insertion, the catheters were removed 1 hour before administration of a scheduled heparin dose. In four patients, blood was aspirated through the epidural needle following placement in the epidural space. The needle was withdrawn, and the patients were given general anesthesia on the following day. No patients developed signs of epidural or subarachnoid hematoma. Similar findings have been reported by Matthews and Abrams,[18] who administered intrathecal morphine through a 20- to 25-gauge needle to 40 cardiac surgical patients 50 minutes before heparinization. Again, no neurologic sequelae were noted postoperatively.

Ruff and Dougherty[28] studied 342 patients who received a diagnostic lumbar puncture (with a 20-gauge needle) for evaluation of acute cerebral ischemia and were subsequently anticoagulated. Patients were evaluated neurologically. Seven patients developed documented spinal hematomas (five with paraparesis, two with severe back pain). Eighteen patients complained of radicular pain lasting more than 48 hours. The authors identified traumatic needle placement (bloody CSF), initiation of anticoagulation within 1 hour of the lumbar puncture, or aspirin treatment at the time of lumbar puncture as being risk factors in the development of spinal hematoma in anticoagulated patients. The amounts of anticoagulant used and results of clotting studies were not reported.

The use of regional anesthesia in patients on low-dose heparin (heparin, 5000 U subcutaneously every 8–12 hours) has also been questioned and remains largely unstudied. In a study of 30 patients on low-dose heparin (5000 U subcutaneously every 8 hours) after undergoing hip replacement, the activated thromboplastin time was measured daily 4 hours after a heparin dose for 9 days. The authors encountered a wide variation in the percentage of patients with an activated thromboplastin prolongation time of greater than 50 seconds, ranging from 5% to 37% with a mean of 21%.[24] This wide variation in response to low-dose heparin makes it difficult to formulate a generalized recommendation regarding regional anesthesia. Allemann et al[1] studied 187 patients who received 5000 U of heparin subcutaneously preoperatively and postoperatively and were operated on under spinal or epidural anesthesia. There were no reported cases of hematoma in this group. Lowson and Goodchild[16] reported 99 epidural and 37 spinal anesthetics performed 2 hours after 5000 U of heparin was subcutaneously administered. Heparin prophylaxis was continued postoperatively including the time the catheter was removed. There were no neurologic complications. Epidural blood vessel puncture with the needle or catheter occurred with an estimated incidence of 5%.

There are at least two reported cases of epidural hematoma occurring in patients on low-dose heparin. In the first case, a diagnostic lumbar puncture was performed on a renal allograft recipient receiving prophylactic anticoagulation therapy (heparin, 5000 U subcutaneously every 8 hours). The patient subsequently developed urinary retention and showed a defect of the posterior lumbrosacral spinal cord on myelogram consistent with spinal hematoma.[4] No surgical procedure was performed, and the patient subsequently died of a myocardial infarction. In another patient receiving 5000 U of heparin every 12 hours prophylactically, an epidural catheter was placed for chronic pain relief. Blood was encountered during catheter placement and an epidural hematoma with complete paraplegia developed over 3 hours. Surgery to improve the neurologic dysfunction was unsuccessful.[23]

The conflicting results of these studies and the rarity of this complication make it difficult to assess the relative risk and contributing variables of spinal hematoma associated with regional anesthesia in patients on anticoagulant therapy. It is important to note that even in a large series, the finding of zero events does not mean the risk is zero, but rather indicates the statistically expected variable incidence of a relatively infrequent event. Possible risk factors contributing to increased risk of spinal hematoma in patients who undergo regional anesthesia and receive perioperative anticoagulation include heparinization within 1 hour of needle placement, concomitant antiplatelet therapy, traumatic needle placement, preexisting coagulopathy or thrombocytopenia, and absence of monitoring the anticoagulant activity.[21, 22, 26, 28]

THROMBOLYTIC THERAPY

Fibrinolysis is frequently used for treatment of pulmonary embolism, deep venous thrombosis, and peripheral artery occlusion. Although intraoperative anticoagulation with heparin appears relatively safe if epidural catheters are inserted before anticoagulation, the risk of developing spinal hematomas in patients receiving regional anesthesia who receive subsequent thrombolytic agents is less well defined.[21, 26]

Thrombolytic agents such as urokinase, streptokinase, and recombinant tissue type plasminogen activator actually lyse fibrin clots that have already formed. Clot lysis leads to elevation of fibrin degradation products, which themselves have anticoagulant effects by interfering with platelet fibrinogen receptors and inhibiting platelet aggregation.[10] Exogenously administered plasminogen activators also affect circulating plasminogen, leading to decreased levels of both plasminogen and fibrinogen. After thrombolytic treatment, fibrinogen and plasminogen levels are maximally depressed at 5 hours and remain decreased for more than 24 hours.[25] In a study involving 290 patients treated with thrombolytic therapy, who were subsequently heparinized for acute myocardial infarction, 32% of the patients suffered hemorrhagic events, usually (70%) involving the site of catheterization or vascular puncture.[25] The authors recommended avoiding invasive procedures in patients receiving thrombolytic therapy.

Dickman et al[5] reported a case of a patient with femoral artery occlusion who received an epidural anesthetic for surgical placement of an intraarterial catheter. A urokinase infusion was initiated through the catheter postoperatively. Three hours later, the patient complained of back pain and a groin hematoma was noted at the catheter placement site. Both the epidural and intraarterial catheters were then removed; however, the back pain persisted and paraplegia developed. Myelography revealed an epidural hematoma from T12 to L4. Emergency decompressive laminectomy was performed resulting in full neurologic recovery within 3 days.

ANTIPLATELET THERAPY

Orthopedic patients undergoing major joint surgery often have chronic musculoskeletal pain or underlying inflammatory disease, such as rheumatoid arthritis, and are frequently medicated with antiplatelet drugs preoperatively. Antiplatelet therapy, including such medications as aspirin, naproxen, piroxicam, and dipyridamole, has been considered a relative contraindication to regional anesthesia by some authors due to the associated prolongation of the bleeding time and theoretically greater risk of hematoma formation.[22]

It has been suggested that the Ivy bleeding time is the most reliable predictor of abnormal bleeding in patients receiving antiplatelet therapy.[27] However, the "postaspirin" bleeding time is not always a reliable indicator of platelet function.[9] Although the bleeding time may normalize within 3 days after aspirin ingestion, platelet function may take up to a week to return to normal. Conversely, several studies have failed to show a correlation between aspirin-induced prolongation of the bleeding time and surgical blood loss.[6] Therefore, measurement of an Ivy bleeding time before induction of spinal or epidural anesthesia may not necessarily identify those patients at increased risk for epidural or spinal hematoma. Other nonsteroidal analgesics (naproxen, piroxicam, ibuprofen) produce a short-term defect that normalizes within 3 days.[3]

The risk associated with administration of spinal or epidural anesthesia to a patient receiving antiplatelet therapy remains controversial and largely unstudied. In a study by Owens et al,[22] antiplatelet therapy was implicated in 2 of 34 cases of spinal hematoma occurring after attempted lumbar puncture. Horlocker et al[11] reported 1013 spinal and epidural anesthetics in which antiplatelet medications were taken by 39% of the patients, including 11% of patients who were on multiple antiplatelet drugs. No patient developed signs of spinal hematoma. However, patients on antiplatelet medications showed a higher incidence of minor hemorrhagic complications (blood aspirated through the spinal or epidural needle or catheter). In addition, increased age and an epidural (but not a spinal) anesthetic technique, when occurring simultaneously, were also associated with an increase in the incidence of minor hemorrhagic events. Although aspiration of blood through the spinal or epidural needle may not imply an increased risk for spinal hematoma, 80% of spinal hematomas occurring after lumbar puncture occurred in patients with evidence of hemostatic abnormality and in 62% the needle placement was described as difficult or traumatic.[22]

SUMMARY

Regional anesthesia can be safely performed in patients receiving anticoagulant or antiplatelet therapy as attested by studies reported by Rao and El-Etr,[26] Horlocker et al,[11] and Odoom and Sih.[21]

Therefore, based on the available information, we believe the following recommendations are appropriate:

1. It is generally agreed that in the absence of extraordinary indications, spinal and epidural anesthesia are contraindicated

in patients within 24 hours of receiving thrombolytic therapy, having known coagulopathies, or having significant thrombocytopenia.

2. Although the data by Odoom and Sih[21] are reassuring, central neuraxis blockade should probably be avoided in fully anticoagulated patients. However, patients who have received only one or two doses of an oral anticoagulant will not have an increased prothrombin time and may safely undergo regional anesthesia. A prothrombin time may be measured before needle placement if necessary.
3. Patients fully anticoagulated with a continuous heparin infusion should have the infusion discontinued 4 to 6 hours before needle or catheter placement. Subcutaneous low-dose heparin should also not be administered within 4 to 6 hours of a spinal or epidural anesthetic to allow for normalization of the activated partial thromboplastin time. Laboratory verification may be performed before initiation of regional blockade.
4. Epidural or spinal anesthesia followed by systemic heparinization is probably safe, provided adequate precautions are taken.[18, 26] Heparinization should not be initiated for at least an hour after needle placement.[18, 28] In addition, patients also receiving antiplatelet medications who will undergo subsequent heparinization appear to be at increased risk for spinal hematoma and need to be followed closely. Rao and El-Etra[26] recommended careful monitoring of the activated clotting time during heparinization. If needle placement is traumatic or difficult, the decision to proceed with surgery should be reevaluated. Removal of an indwelling epidural catheter in a patient receiving intravenous or subcutaneous heparin should occur 4 to 6 hours after the last heparin dose, and anticoagulation should not be initiated for at least 1 hour after catheter removal.
5. Epidural and spinal anesthesia can be safely performed in a patient receiving antiplatelet therapy.[11] Patients with a history of bleeding or bruising may be further evaluated with a preoperative bleeding time.
6. The use of small-gauge needles and the midline approach (thereby avoiding the lateral aspect of the epidural venous plexus) allows more atraumatic needle placement. Epidural catheters should not be inserted more than 3 to 4 cm into the epidural space in order to minimize trauma to the epidural venous structures.
7. Short-acting local anesthetics should be used in patients at increased risk in order to promptly evaluate their neurologic status postoperatively. Likewise, an epidural blockade should be allowed to regress sufficiently before initiating a continuous local anesthetic infusion for postoperative analgesia. A narcotic rather than local anesthetic infusion would allow continuous monitoring of neurologic function and may be a more prudent choice in these patients.

It is also worth noting that epidural hematomas have also occurred spontaneously in patients on anticoagulant or antiplatelet medications in the absence of trauma or needle placement.[15] The decision to perform spinal or epidural anesthesia on a patient receiving these medications should be made on an individual basis, weighing the risks of hemorrhagic complications and benefits of regional anesthesia for a specific patient. The patient's history should be reviewed to discover any underlying medical conditions with associated bleeding tendencies that would increase the risk. Because it is difficult to predict an individual patient's response to antiplatelet or anticoagulant therapy, laboratory verification may be helpful before initiation of spinal or epidural anesthesia (Table 1). It is most useful clinically to evaluate coagulation parameters that are specific to the clotting defect expected such as the prothrombin time in patients on oral anticoagulants or the activated thromboplastin time in heparinized patients. Although the role of tests such as the thromboelastogram, which measure overall coagulation function, has not been defined at this time, they may prove useful in the future. Needle and catheter placement should be accomplished as atraumatically as possible, and subsequent anticoagulation should be carefully monitored to minimize hemorrhagic complications. The patient should be monitored closely in the perioperative period for early signs of cord compression such as backache or neurologic dysfunction, and any clinical or radiologic evidence of cord compression should be followed by an immediate decompressive laminectomy because recovery is unlikely if surgery is delayed for more than 12 hours.[8]

Table 1. PHARMACOLOGIC PARAMETERS OF ANTICOAGULANTS AND ANTIPLATELET AGENTS

Agent	Effect on Coagulation Parameters			Time to Peak Effect	Time to Normal Hemostasis Posttherapy	Comments
	BT	PT	APTT			
Heparin, intravenous	↑	↑	↑ ↑ ↑	Minutes	4–6 hours	Delay heparinization for 1 hour after needle placement
Heparin, subcutaneous	↑	↑	↑ ↑	40–50 minutes	4–6 hours	Monitor ACT, APTT
Warfarin	—	↑ ↑ ↑	↑	4–6 days (3 days with loading dose)	4–6 days	Monitor PT
Aspirin	↑ ↑ ↑	—	—	Hours	7 days	Increased age with epidural technique may increase incidence of minor hemorrhage following needle placement
Other NSAID	↑ ↑ ↑	—	—	Hours	3–5 days	
Thrombolytic agent	↑ ↑ ↑	↑	↑	Minutes	1–2 days	Usually heparinized in addition. Monitor closely

Abbreviations: BT = bleeding time; PT = prothrombin time; APTT = activated thromboplastin time; ACT = activated clotting time; NSAID = nonsteroidal antiinflammatory drug.

References

1. Allemann BH, Gerber H, Gruber UF: Rückenmarksnahe Anaesthesie und subkutan verabreichtes low-dose heparin-dihydergot zur thromboembolieprophylaxe. (Perispinal anesthesia and subcutaneous administration of low-dose heparin-dihydergot for prevention of thromboembolism). Anaesthetist 32:80–83, 1983
2. Cousins MJ, Wright CJ: Graft muscle, skin blood flow after epidural block in vascular surgical procedures. Surg Gynecol Obstet 133:59–64, 1971
3. Cronberg S, Wallmark E, Soderberg I: Effect on platelet aggregation of oral administration of 10 non-steroidal analgesics to humans. Scand J Haematol 33:155–159, 1984
4. Dean WM, Woodside JR: Spinal hematoma compressing cauda equina. Urology 13:575–577, 1979
5. Dickman CA, Shedd SA, Spetzler RF, et al: Spinal epidural hematoma associated with epidural anesthesia: Complications of systemic heparinization in patients receiving peripheral vascular thrombolytic therapy. Anesthesiology 72:947–950, 1990
6. Ferraris VA, Swanson E: Aspirin usage and perioperative blood loss in patients undergoing unexpected operations. Surg Gynecol Obstet 156:439–442, 1983
7. Gustafson H, Rutberg H, Bengtsson M: Spinal haemotoma following epidural analgesia. Anaesthesia 43:220–222, 1988
8. Harik SI, Raichle ME, Reis DJ: Spontaneously remitting spinal epidural hematoma in a patient on anticoagulants. N Engl J Med 284:1355–1357, 1971
9. Hindman BJ: Usefulness of the post-aspirin bleeding time. Anesthesiology 64:368–370, 1986
10. Hirsch DR, Goldhaber SZ: Bleeding time and other laboratory tests to monitor the safety and efficacy of thrombolytic therapy. Chest 97:1245–1315, 1990
11. Horlocker TT, Wedel DJ, Offord KP: Does preoperative antiplatelet therapy increase the risk of hemorrhagic complications associated with regional anesthesia? Anesth Analg 70:631–634, 1990
12. Joist JH, Sherman LA (ed): Venous and Arterial Thrombosis Pathogenesis, Diagnosis, Prevention, and Therapy. New York, Grune & Stratton, 1979
13. Keith I: Anaesthesia and blood loss in total hip replacement. Anaesthesia 32:444–450, 1977
14. Linn BJ, Mazza JJ, Friedenberg WR: The treatment of venous thromboembolic disease. Postgrad Med 79:171–180, 1986
15. Locke GE, Giorgio AJ, Biggers SL, et al: Acute spinal epidural hematoma secondary to aspirin-induced prolonged bleeding. Surg Neurol 5:293–296, 1976
16. Lowson SM, Goodchild CS: Low-dose heparin therapy and spinal anesthesia. Anaesthesia 44:67–68, 1989
17. Malinovsky NN, Kozlov VA (eds): Anticoagulant and Thrombolytic Therapy in Surgery. St. Louis, Mosby, 1979
18. Matthews ET, Abrams LO: Intrathecal morphine in open heart surgery. Lancet 2:543, 1980
19. Modig J, Borg T, Karlström G, et al: Thromboembolism after total hip replacement: Role of epidural and general anesthesia. Anesth Analg 62:147–180, 1983
20. Ockelford P: Heparin 1986 indications and effective use. Drugs 31:81–92, 1986
21. Odoom JA, Sih IL: Epidural analgesia and anticoagulant therapy. Anaesthesia 38:254–259, 1983
22. Owens EL, Kasten GW, Hessel EA: Spinal hematoma after lumbar puncture and heparinization. Anesth Analg 65:1201–1207, 1986
23. Parnass SM, Rothenberg DM, Fischer RL, et al: Spinal anesthesia and minidose heparin. JAMA 263:1496, 1990
24. Poller L, Taberner DA, Sandilands DG, et al: An evaluation of APTT monitoring of low-dose heparin dosage in hip surgery. Thromb Haemostas 47:50–53, 1982
25. Rao AK, Pratt C, Berke A, et al: Thrombolysis in myocardial infarction trial—Phase I. J Am Coll Cardiol 11:1–11, 1988
26. Rao TLK, El-Etr AA: Anticoagulation following placement of epidural and subarachnoid catheters: An evaluation of neurologic sequelae. Anesthesiology 55:618–620, 1981

27. Rapaport SI: Preoperative hemostatic evaluation: Which tests if any? Blood 61:229–231, 1983
28. Ruff RL, Dougherty JH: Complications of lumbar puncture followed by anticoagulation. Stroke 12:879–881, 1981
29. Spurny OM, Rubin S, Wolff JW, et al: Spinal epidural hematoma during anticoagulant therapy. Arch Intern Med 114:103–107, 1964

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ADJUVANTS IN EPIDURAL AND SPINAL ANESTHESIA

M. S. Batra, MD, FRCPC

Neural blockade with resultant analgesia or anesthesia typically follows when a local anesthetic is applied to a nerve fiber. Salient characteristics of such a pharmacologic event include speed of onset, quality or depth of blockade, and its total duration. These and other properties distinguish one local anesthetic from another. Agents that induce neural blockade quickly usually have a short duration of action and those with longer duration typically are slow to produce anesthesia. Onset of blockade occurs when the local anesthetic reaches the interior of the axoplasm in sufficient quantity, and blockade of conduction is maintained as long as the local anesthetic remains at the site in its active form. These properties can be altered somewhat and to variable degree by modification of the local anesthetic. The agents or forces that bring about these changes are referred to as adjuvants. Need for these modifiers is greater with epidural neural blockade because the local anesthetic has to overcome several barriers before reaching the neural tissue or be prevented from being removed quickly, which may terminate its action. During spinal anesthesia, the need for overcoming such barriers may be less important; however, there are other reasons that make the use of adjuvants very helpful in this setting. Adjuvants, in addition, affect the quality of analgesia and anesthesia by influencing nociception in ways other than by an effect on neural conduction. Most of the clinically useful adjuvants either alter the physicochemical properties of the local anesthetics or enhance their analgesic and anesthetic properties by additional pharmacologic activity peculiar to the individual agent.

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ALTERATIONS OF PHYSICOCHEMICAL PROPERTIES OF LOCAL ANESTHETICS

Carbonation and Alkalinization

Local anesthetic drugs typically produce their desired effect by reaching the interior of neural tissue. The onset of their effect is hastened, quality is improved, and duration prolonged somewhat, if a sufficient amount of drug reaches the targeted area quickly. It is the lipid-soluble undissociated base form of the drug that penetrates the neural membrane to reach the interior of the axoplasm. The pharmacologic effect, blockade of nerve conduction, however, is produced by the water-soluble dissociated cationic form. The degree of dissociation is determined by the Henderson-Hasselbach equation and is dependent on the drug's dissociation constant (pKa), at which the drug is present in half undissociated and half dissociated form. The pKa of commonly used local anesthetics is between 7.7 and 8.9. Lidocaine and bupivacaine have a pKa of 7.9 and 8.1, respectively. Most commercial preparations of local anesthetics are quite acidic (pH ranging from 4.2–6.5) to improve stability of the drug and thus prolong its shelf life. At this range of pH, less drug is available in the undissociated base form, which is required for transfer across the perineural sheath and neural membrane. Agents influencing the degree of dissociation should therefore have an effect on the onset and degree of neural blockade. Dissolution of carbon dioxide (CO_2) in the local anesthetic solution influences the local anesthetic in the following ways: (1) When an ampule is opened, some CO_2 diffuses out. This effervescence raises the pH of the solution, thereby increasing the amount of local anesthetic in its base form. (2) On injection of a carbonated solution around a nerve, CO_2 diffuses through neural membrane freely and enters the interior of the nerve where it decreases the pH. This increases dissociation of the local anesthetic, the passage of which has already been facilitated, and the increased amount of active cationic form of local anesthetic, now in somewhat of an ionic trap, enhances neural blockade. Carbon dioxide has also been shown to have a stabilizing effect on excitable tissue membranes.[54] This phenomenon per se might influence nerve conduction. Whether carbon dioxide enhances local anesthetic effect by simply altering the degree of dissociation, thereby affecting uptake and entrapment, or by mechanisms that significantly influence nerve conduction, still needs to be elucidated. There is some experimental evidence that points toward the "facilitated uptake and ion trapping" as the main mechanism for enhancement of local anesthetic function. Work done with n-butanol, a nonionizable local anesthetic, has shown that carbonation alone fails to affect local anesthetic action to the same degree.[22] A solution of carbonated lidocaine has a pH of 6.5 and partial pressure of CO_2 (P_{CO_2}), around 700 mm Hg. Alkalinization with sodium bicarbonate also increases the P_{CO_2} modestly to 100 mm Hg.

In earlier clinical studies, carbonation of lidocaine and prilocaine has been shown not only to enhance onset of epidural anesthesia but also to improve the quality and extent of sensory and motor blockade.[12] At closer examination, the only criticism of the studies is that they were not randomized and blinded, which may have influenced the observations made by the investigators. However, the work by Nickle et al,[72] which was double blinded, did confirm the observations made by others. Martin et al[59] and Morison[69] were able to demonstrate improved quality of sensory anesthesia, but failed to confirm faster onset or increased duration. Clinical studies with carbonated local anesthetics in peripheral nerve blocks also appear to show an enhanced action of local anesthetics by increasing rate of onset and the extent of the block produced.[14, 20] The addition of CO_2 to bupivacaine has not been beneficial to the same extent.[17] Unfortunately, carbonated solutions of local anesthetics are not yet available for clinical use in the United States. Further studies, demonstrating the usefulness and lack of adverse effects of carbonation, are therefore clearly indicated.

Greater availability of local anesthetic in its undissociated base form can be easily accomplished, however, by the simple addition of bicarbonate to most solutions of local anesthetics, just before injection. Alkalinization in this way appears to produce a much more rapid onset of action following injection of lidocaine into the epidural space.[32] The quality of sensory blockade with mepivacaine for epidural anesthesia was shown by Galindo[42] to be greatly improved. Experience with bupivacaine has not produced consistent results. The onset of analgesia was found to be more rapid in parturients as reported by McMorland et al,[61] whereas in a recent blinded study by Benhamou et al,[6] no difference of clinical significance was noted when 0.5% bupivacaine was modestly pH adjusted (from 4.8 and 5.38 to 6.68 and 6.87) for use during epidural anesthesia for cesarean section. A similar lack of effect with pH adjustment of bupivacaine was shown by Stevens and coworkers[84] in nonpregnant patients receiving epidural anesthesia for knee surgery. Upward adjustment of pH, however, should be done very carefully, as excessive alkalinization causes the local anesthetic to precipitate.[7, 49] This is especially common with bupivacaine and etidocaine. The amount of sodium bicarbonate required to raise the pH of commonly used local anesthetic solutions above 7 is listed in Table 1.

Vascular uptake of lidocaine and bupivacaine from the epidural space has been shown to be enhanced with carbonation.[3, 60] Greater availability of unionized drug base and the vasodilating property of CO_2 may account for the greater uptake of local anesthetic. This might increase the likelihood of local anesthetic toxicity with large doses or following an accidental intravascular injection of a smaller amount. I have personally observed CNS toxicity on two separate occasions with less than 100 mg of carbonated lidocaine, which was unintentionally administered intravascularly during induction of an epidural block in nonpregnant patients, when use of a test dose was not a common practice. Simple alkalinization with the addition of sodium bicarbonate has not been associated with increased vascular uptake of lidocaine from the epidural space in parturients undergoing cesarean section.[32]

Table 1. AMOUNT OF SODIUM BICARBONATE REQUIRED TO RAISE THE PH OF COMMONLY USED LOCAL ANESTHETIC SOLUTIONS TO ABOVE 7

Agent (%)	Volume of Local Anesthetic Solution (mL)	Amount of 8.4% Sodium Bicarbonate (1 mEq/mL)
Lidocaine 1.0	10	1.2
Lidocaine 1.5	10	1
Lidocaine 2.0	10	0.8
Mepivacaine 1.0	10	1
Mepivacaine 1.5	10	0.8
Mepivacaine 2.0	10	0.7
Chloroprocaine 2.0	30	1
Chloroprocaine 3.0	30	1
Bupivacaine 0.25	20	0.12
Bupivacaine 0.5	20	0.08
Bupivacaine 0.75	20	0.04

Warming of Local Anesthetic

Local anesthetics for most blocks are usually injected at room temperature, which in most operating rooms is somewhere between 65°F and 72°F. In the past, when dibucaine (Nupercaine) was a popular anesthetic for spinal anesthesia, it was common practice to warm the local anesthetic to enhance onset, and perhaps, duration. This simple modification was recently investigated with regard to bupivacaine, and it was found that warming the solution to 100°F significantly increased the speed of onset and extent of spread and improved the quality of epidural blockade in pregnant patients, whereas duration of anesthesia and degree of motor block were not appreciably altered.[48, 63] These beneficial effects of warming have not been studied for other agents. The mechanism by which warming enhances neural blockade is not well understood, but it appears that raising the temperature produces an effect that is similar to alkalinization and carbonation. Warming the solution of bupivacaine and intravenous fluids has also been shown to decrease the annoying side effects of shivering after epidural anesthesia in parturients.[48, 62] Needless to say, however, maintaining the temperature of local anesthetic solution or warming it precisely to 100°F just before injection is not an easy task in a busy practice situation, and great care must be exercised to ensure that the solution does not get overly hot.

Dextrose and Water

These agents are used in spinal anesthesia primarily to modify the density of the local anesthetic solution. They do not affect neurologic function by themselves.

Dextrose in varying amounts is added to a solution to make it hyperbaric. This facilitates local anesthetic spread by gravity to dependent areas in the subarachnoid space. The effect on baricity appears to be dose dependent. The minimal concentration of dextrose that renders a local anesthetic solution slightly hyperbaric is 0.83%.[4] For a solution to be reliably hyperbaric the baricity must be 1.0015 or greater. Most clinicians employ a much more hyperbaric solution, containing dextrose in concentrations varying from 5% to 10%. These highly hyperbaric mixtures, although benign following a single injection through a needle, may not be totally harmless when administered slowly via an intrathecal catheter.[78] Overly hyperbaric solution when introduced extremely slowly, as would occur while injecting through a microbore catheter, may aid in concentrating a large amount of local anesthetic around an unprotected nerve. Such supersaturation of neural tissue with local anesthetics may produce neurotoxicity.

Water is mixed with a spinal local anesthetic solution to decrease its baricity. A solution must have a baricity of 0.9990 to be consistently hypobaric. The addition of water not only makes the solution lighter than CSF, it decreases the concentration and increases the volume, which have an effect on the intensity and extent of neural blockade. A very dilute solution produces a differential block, characterized by autonomic blockade, minimal sensory anesthesia, and no effect on the motor function.

PHARMACOLOGIC ENHANCEMENT OF ANALGESIA AND ANESTHESIA PRODUCED BY LOCAL ANESTHETICS

Epinephrine and Other Sympathomimetics

The use of adjuvants to prolong the duration of neural blockade dates back to 1885, only a year following the first clinical use of cocaine. A mechanical tourniquet applied proximal to the area of local anesthetic application not only prolonged the duration but also intensified the degree of neural blockade. In ophthalmologic therapeutics it had been noted that epinephrine prolonged the action of locally applied agents. Epinephrine as an adjuvant in spinal anesthesia was first employed with cocaine at the turn of the century by Braun.[10, 11] He used the drug in varying concentrations and noted undesirable systemic side effects with doses greater than 0.5 mg, thereby establishing a therapeutic-to-toxicity ratio in the early days of its use for this purpose.

Epinephrine has been extensively studied since it became available in a pure form in 1903. It has primarily been employed as an adjuvant to (1) prolong the duration of neural blockade; (2) reduce and perhaps delay the systemic toxicity of local anesthetics; (3) increase the intensity of analgesia and anesthesia; (4) reduce vascularity in the area of injection, thereby decreasing blood loss and improving surgical conditions; (5) be a marker in a small "test dose" that warns against a direct intravascular injection; and (6) increase the quality and extent of neural blockade. Secondarily, it has been observed that the concomitant use of epinephrine (7) reduces the incidence of tachyphylaxis and (8) makes it frequently unnecessary to employ continuous catheter techniques that invariably prolong the block procedure and increase the risks associated with regional anesthesia.

Considerable scientific evidence has accumulated to substantiate some of these claims, but many of its indications are still being examined in depth with regard to the therapeutic benefits when balanced against real or potential toxic side effects.

Prolongation of Duration of Neural Blockade

Duration of action of any drug is primarily determined by the availability of that drug in a critical amount at its site of action. The longer a sufficient amount of the drug remains at the site the longer will be the duration of its action. This is well exemplified by local anesthetics. Epinephrine, by virtue of its vasoconstrictor property, reduces blood flow to the area and slows down vascular uptake. The duration is prolonged more in areas with abundant vascularity as retardation of vascular uptake is enhanced to a greater extent.

Prolongation of epidural and spinal anesthesia occurs to significant degree with intermediate duration lidocaine[16] and mepivacaine.[18, 52] Such prolongation is not as apparent with the longer acting agents bupivacaine and etidocaine. This may be due to their greater affinity for neural tissue (higher lipid solubility), and once bound, the drugs are dissociated slowly, regardless of local vascularity. However, bupivacaine has been shown to produce longer epidural blockade in the parturient.[57]

Once the duration is prolonged sufficiently, it becomes possible to perform surgical procedures with single injection epidural anesthesia, thus obviating the need for catheter placement for reinjection after a short interval. This is beautifully substantiated by experience with anesthesia for back surgery, which, at our institution, has been and is performed under epidural anesthesia with 0.5% to 0.75% bupivacaine and epinephrine as an adjuvant.

A secondary benefit of increased duration is that in an attempt to maintain the block at the same level fewer reinjections are required over a given period of time. This results in reduced drug accumulation, thereby reducing systemic toxicity.

There is evidence that epinephrine influences the duration of neuraxially administered opioids as well. Analgesia following epidural administration of morphine is of longer duration with epinephrine[13] and a similar increase has also been reported with simultaneous use of fentanyl and epinephrine intrathecally.[58] In addition, the latter work was associated with a marked decrease in the incidence of pruritus.

Adjuvants like epinephrine and phenylephrine prolong the duration of spinal anesthesia with most anesthetic agents as well.[8, 33]

Although this prolongation has been reaffirmed for tetracaine,[27, 82] there appears to be some controversy with regard to a significant difference following lidocaine[24, 83] and bupivacaine.[25, 76] The discrepancies in results appear to be related to differences in methodologies. Studies reporting no prolongation used two-segment regression as their end-point, whereas when anesthesia in more distal segments, lumbar and sacral, is compared, definite and significant prolongation has been noted.[1, 56, 66, 67] It has been noted that the motor block following subarachnoid injection of bupivacaine develops more rapidly when epinephrine is used as an adjuvant.[1] Our clinical experience in the outpatient setting has also shown that not only is there prolongation of surgical anesthesia, which is somewhat related to a greater spread of subarachnoidally administered drugs, but the time to ambulation and discharge is also longer when epinephrine is used with lidocaine and procaine.

In an attempt to prolong the duration of spinal anesthesia even longer than that following epinephrine as an adjuvant, phenylephrine has been used with variable results. The concept and widely held clinical belief that phenylephrine prolongs sensory and motor blockade following tetracaine to a greater extent than epinephrine was challenged by Concepcion et al.[27] These investigators examined the effects of equipotent, yet low doses of the two vasoconstrictors on the duration of spinal anesthesia with tetracaine and found that there was no significant difference. A subsequent double-blinded study, employing higher and clinically recommended doses, showed that phenylephrine does prolong the duration of sensory anesthesia with tetracaine to a much greater degree.[19] Ephedrine and other vasoconstrictors have also been employed to slow regression of spinal anesthesia, but the results have not been universally satisfactory.[8]

Reduction and Delay of Systemic Absorption of Local Anesthetic

Systemic absorption following epidural injection of local anesthetic is surprisingly rapid. This is primarily related to the dose and somewhat to the site of injection in the epidural space. It has been noted that systemic absorption from the sacral epidural space (caudal) is much faster than that following lumbar injection. The rate of absorption and the peak levels achieved are significantly lower when epinephrine is used as an adjuvant. These effects are greater with lidocaine and mepivacaine and somewhat less with bupivacaine and etidocaine. Clinically, therefore, employment of vasoconstrictors helps reduce systemic toxicity from local anesthetics, allows a greater dose to be administered when required, and decreases placental transfer.

Increase in Intensity of Analgesia and Anesthesia

Intensity of neural blockade is in direct proportion to the amount of local anesthetic available at its site of action, which is in the interior of the nerve fiber. Epinephrine has been shown to facilitate and thereby increase the intraneural uptake of lidocaine.[38] In addition, it has been observed that α_2-agonists (epinephrine, clonidine) modulate the neuronal response to noxious stimuli, and intensification of analgesia and anesthesia has been shown to occur in animal preparations[31] as well as in clinical studies.[34, 82] This is discussed in greater detail later in this article.

Clinical application of this property ensures an improved quality of analgesia and anesthesia. The dilemma of increased duration, when not desirable, can be minimized by reducing the total dose of local anesthetic. This requires some fine tuning, but our experience has shown that the dose of local anesthetic can easily be reduced by about 30% to 50% for spinal anesthesia.

As a Marker in a Test Dose

Epinephrine has been recommended as an adjuvant in a test dose, when, by virtue of its systemic cardiovascular effects, it warns against injection of a large and potentially toxic dose of local anesthetic in the event of an unintentional intravascular administration. The subject of test dose is reviewed extensively elsewhere in this issue; however, the use of epinephrine for this indication in my practice can be summarized as follows:

1. Inclusion of 10 to 15 μg of epinephrine in a test dose is a safe recommendation.
2. The test dose procedure must be used correctly for it to provide useful information.
3. Intravascular injection of epinephrine produces *objective* and *subjective* changes, which must be considered together.
4. When in doubt, administration of a test dose should be repeated after about 3 minutes.
5. A negative test dose does not guarantee against an intravascular injection. However, it drastically reduces the likelihood of its occurrence.
6. The risk of using epinephrine in a test dose in a given patient must be weighed against the potential risks associated with possible intravascular local anesthetic administration. Fortunately, there is seldom a situation when the use of a such a small dose of epinephrine is truly contraindicated.
7. A test dose containing epinephrine is only necessary before an injection of a local anesthetic in a dose that is potentially toxic in the event of an accidental intravascular injection. In practice, therefore, it is seldom necessary to include epinephrine in a test dose while inducing epidural analgesia for labor. The dose of local anesthetic is usually small and the ensuing analgesia within a short period of time (10–15 minutes) assures a satisfactory epidural injection.

The evolution of these guidelines has taken time (nearly 10 years), and we have been able to virtually eliminate systemic toxicity following epidural analgesia and anesthesia in our high volume regional anesthesia practice.

Reduction in the Incidence of Tachyphylaxis

Reduced effectiveness of repeat injections in an intermittent epidural technique has been referred to as *tachyphylaxis*. This is a form of acute tolerance that appears to develop when an existing block is allowed to wear off, even minimally. Maintaining an effective blockade with a continuous infusion of local anesthetic does not increase the dose requirement over time. The phenomenon of tachyphylaxis can be circumvented or delayed by the use of (1) longer-acting local anesthetic agents; (2) reinjections given at regular and timed intervals, ensuring sufficient intraneural concentration of local anesthetic, which will maintain constant conduction blockade; and (3) increasing the duration and intensity of neural blockade by the addition of adjuvants like epinephrine.[16] It appears that not only is there prolongation of duration of a given dose, but the speed of decay of neural blockade is slowed down as well, allowing the subsequent reinjected dose to reblock or maintain the previous level of analgesia and anesthesia.

Optimal Concentration and Dose of Epinephrine as an Adjuvant

Minimal effective concentration of epinephrine for use in epidural anesthesia is around 2.5 μg/mL (1:400,000). It appears that increasing the dose beyond 5 μg/mL (1:200,000) provides no greater beneficial effect and invariably increases the likelihood of side effects and complications following systemic absorption. It has also been determined that an intravenous administration of a bolus of 10 to 15 μg of epinephrine is required to produce clinical effects that provide observable or measurable effects.[45, 65] This is the amount present in 2 to 3 mL of a local anesthetic solution containing epinephrine in a concentration of 1:200,000, as recommended for use as a test dose during epidural anesthesia.

Commercial preparations of local anesthetics with epinephrine are quite acidic (pH, around 4.0) as epinephrine is rapidly inactivated in an alkaline solution. In such an acidic medium, as discussed previously, very little local anesthetic is available in the unionized base form for easier penetration of neural tissue. Most clinicians, therefore, add epinephrine to a plain local anesthetic solution that usually has a much higher pH (around 6.0). Such a fresh formulation also provides flexibility in optimizing the dose of epinephrine to minimize side effects, without altering the concentration of local anesthetic. It has also been observed that the onset of analgesia is significantly more rapid with fresh addition of epinephrine as compared with that following the use of commercial preparations of lidocaine with epinephrine.[32]

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The minimal effective concentration of epinephrine for spinal anesthesia appears to be around 0.2 mg. Larger doses of up to 0.5 mg have been used that significantly prolong the duration of anesthesia with tetracaine and bupivacaine.[19] A greater amount of epinephrine is required for spinal anesthesia, as CSF in the spinal subarachnoid space (around 25–35 mL in an average adult) dilutes the drug.

Systemic Effects of Epinephrine (with Local Anesthetic) Injected into the Epidural Space

Epinephrine is absorbed surprisingly rapidly from the epidural space and produces effects that are similar to a slow intravenous infusion of around 2 to 3 μg/min. The overall effect on the cardiovascular system is quite complex owing to its direct effects being drastically modified by the local anesthetic induced sympathetic blockade and the effects of local anesthetic on the heart and vascular smooth muscle in general. Epinephrine in itself produces stimulation of α- and β-adrenergic receptors. Stimulation of the β_1-receptors in the myocardium is associated with increased contractility, enhancement of the pacemaker and conducting activity, increasing heart rate, and irritability. Cardiac output is increased. The systolic blood pressure increases slightly, followed by a gradual decrease with the onset of epidural anesthesia. The degree of hypotension is usually proportional to the extent of sympathetic blockade, which affects peripheral resistance and heart rate. The hemodynamic effects of thoracolumbar sympathetic blockade usually overshadow the direct effects of epinephrine.

Regional blood flow can be summarized as follows: (1) Coronary blood flow is affected by increased aortic pressure, increased diastolic time, and metabolic factors secondary to increased contractility and further modified by the hemodynamic changes produced by the extensive sympathetic blockade. (2) Cerebral blood flow is generally unaffected because autoregulation corrects mild changes in systemic hemodynamics. (3) Renal blood flow is reduced due to renal vasoconstriction. Glomerular filtration rate is somewhat less affected, maintaining adequate urine output. Renin secretion is increased. (4) Pulmonary circulation is affected secondarily, and pulmonary arterial pressure reflects changes in the total peripheral resistance.

The direct cardiovascular effects of epinephrine are magnified when the drug enters the circulation directly while being used in a test dose or the main dose of local anesthetic mixed with epinephrine accidentally finds its way into the blood stream. These are dose related, and from observations in volunteers and patients it has been noted that the effects following the amount present in a test dose are quite transient and do not cause any harm. A systemic injection of 10 to 15 μg of epinephrine, in some patients, produces palpitations, throbbing headache, anxiety, and restlessness. These are more pronounced in anxious and apprehensive subjects; therefore, it is useful to sedate such subjects adequately.

Uterine Smooth Muscle and Blood Flow

Epinephrine inhibits pregnant uterine tone and contractility and the effects are dose related. Clinically, when epinephrine is used in recommended doses, these effects are not only minimal but transient. Uterine blood flow, similarly, is affected, less due to the direct effects of epinephrine, but to the overall effects on the systemic circulation. Wallis et al[92] reported a 14% decrease in uterine blood flow lasting 15 minutes following an epidural injection of 2-chloroprocaine with 60 to 80 μg of epinephrine in normotensive gravid ewes. Jouppila et al[50, 51] and Albright et al,[2] using radioactive xenon in pregnant human subjects, however, found no deleterious effect on intervillous blood flow. The significance of the effects in the mother and the fetus after an intravascular injection of epinephrine in an amount such as that in a recommended test dose has generated considerable debate. Hood et al[47] reported a dose-related reduction in uterine blood flow following a bolus intravenous administration of 5, 10, and 20 μg of epinephrine in gravid ewes, and the effect with the latter two doses lasted more than 3 minutes. Chestnut and coworkers[26] similarly demonstrated a 28% and 44% reduction in uterine artery blood flow velocity following 0.2 and 0.5 μg/kg of epinephrine intravenously in pregnant guinea pigs near term, and such reductions lasted 90 seconds and 4 minutes, respectively. These studies suggest that intravenous boluses of epinephrine in doses similar to those recommended in typical test doses result in significant reductions in the uterine blood flow in the gravid ewes and guinea pigs. These effects are, however, transient and whether similar changes occur in humans is still unknown. Both studies also showed significant increases in maternal blood pressure following intravenous epinephrine. It is well recognized that parturients with pregnancy-induced hypertension are overly sensitive to pressor agents and use of epinephrine in such a setting, from maternal standpoint alone, might be worth considering.

Epinephrine and Spinal Cord Blood Flow

It is generally believed that epinephrine produces some of its beneficial effects by vasoconstriction. There is no clear evidence in the literature, however, that supports such a claim. Porter and coworkers[74] studied the effects on spinal cord and cerebral blood flow following subarachnoid injection of local anesthetics, with and without epinephrine, and found that epinephrine with lidocaine, mepivacaine, or tetracaine failed to show any change in segmental blood flow to the cord. Kozody et al[53] in a similar study showed that subarachnoid injection of lidocaine alone produces spinal cord vasodilation, whereas when epinephrine is injected with lidocaine, such vasodilation fails to occur. Furthermore, they were unable to demonstrate any actual reduction in spinal cord blood flow. It is also appropriate to state that extensive clinical experience in humans over the years attests to the safety of administration of epinephrine with local anesthetics into the subarachnoid space. This statement is further substantiated by the fact that spinal anesthesia traditionally has been used more often in the older patient, with less than optimal vasculature, and the typical response to administration of various local anesthetics, with epinephrine or phenylephrine has not been different than that seen in younger patients. Such claims are unwarranted, however, when these drugs are used incorrectly.

Situations When Epinephrine Should Not Be Used as an Adjuvant

1. Significant hypertension that is poorly controlled may be further aggravated by the use of epinephrine during epidural anesthesia when an accidental intravascular injection occurs. Epinephrine can, however, be used provided necessary steps are taken to ensure that the drug will not be injected directly into the systemic circulation in a large dose. A slow and fractionated injection is very helpful in this situation. Use of epinephrine during spinal anesthesia is not a problem in a patient with hypertensive disease.
2. In a patient with history or presence of tachyarrhythmias, caution must be exercised to prevent a rapid systemic injection of a large dose of epinephrine.
3. The presence of significant coronary artery disease requires that a very careful and meticulous approach be taken to ensure that a large intravascular injection will not take place. The amount of epinephrine in a test dose (10–15 μg) has not been associated with significant problems.
4. Patients on drugs that modify the metabolism or action of catecholamines, i.e., monoamine oxidase inhibitors and tricyclic antidepressants, may be at risk for significant side effects if such agents are employed.

α_2-Adrenergic Agents

It has been known for a long time that when adrenergic agonists are applied to the spinal cord, they produce analgesia. α_2-Adrenergic receptors have been demonstrated to exist on the dorsal horn of the spinal cord.[39] These receptors apparently inhibit the release of the nociceptive neurotransmitter, substance P, or other peptides. The mechanism of action may involve modulation of the role played by cAMP and serotonin. It has also been observed that there is a strong synergism between α_2-agonists and opioids in their ability to produce spinal cord–mediated analgesia.[73]

Clonidine, an α_2-adrenergic agonist, was first used epidurally by Tamsen and Gordh[88] in two patients with intractable pain, demonstrating not only its effectiveness but also the phenomenon of synergism. Eisenach et al[36, 37] reported profound analgesia during phase I studies, following epidural use of clonidine in surgical patients and in patients with intractable cancer pain. Their report indicated that the analgesia produced appeared to be dose related, but enhancement of morphine mediated analgesia was not seen. Others have shown clonidine induced enhancement of analgesia produced by epidural sufentanil.[90]

Shortly thereafter, it was demonstrated that injection of clonidine intrathecally produced intense analgesia in a patient who had become tolerant to intrathecal morphine.[29] The analgesia following such an administration appears to be of long duration (more than 18 hours), which is somewhat similar to that observed with intrathecal morphine. Later, Laugner et al[55] further confirmed the production of profound relief of pain in several patients who had become tolerant to intrathecal morphine.

Racle et al[76, 77] reported on the use of clonidine as an adjuvant during bupivacaine-induced spinal anesthesia. They noted that two-segment regression in the clonidine-treated group was significantly delayed when compared with those treated with epinephrine and the control group. It has also been observed that tourniquet-induced pain is reduced as well when clonidine is added to isobaric bupivacaine during spinal anesthesia. Prolongation of analgesia and motor blockade following tetracaine also has been demonstrated with clonidine, 50 to 150 μg intrathecally.[5, 9, 64] Animal studies have shown that epidural and spinal injection of clonidine does not have a significant effect on the blood flow[35, 43, 44] or histologic structure of the spinal cord.[44]

The potentiation of anesthesia and analgesia following epidural and spinal injections of local anesthetics with epinephrine is further evidence for the analgesic properties of α_2-adrenergic agents.

Opioids

The role of intraspinal (epidural and intrathecal) opioid analgesia in the postoperative period is discussed at length elsewhere in this issue. In addition, opioids by these routes are also being increasingly employed for analgesia during labor, which is discussed in considerable detail in the article by Writer. A brief discussion of their contribution to enhancement of epidural anesthesia for surgery is not out of place here. It is common knowledge that total antinociception is not always achieved during surgery with local anesthetic induced neuraxial blockade. Anesthesia can, in most instances, be intensified by the concomitant use of other adjuvants, as discussed previously, or supplementation may be provided by systemic administration of analgesics, sedatives, or inhalational anesthetics. However, this is not always desirable, and clinicians are forever on the lookout for other alternatives. It is well recognized that opioids suppress nociceptive input at the spinal level by their action on the opiate receptors in the substantia gelatinosa cells in the dorsal horn of the spinal cord. This antinociception at a different site has not only been shown to improve the quality of analgesia during labor and in the postoperative period, with extremely dilute concentrations of local anesthetics, but has been observed during neuraxial anesthesia as well. Alleviation of visceral discomfort with sufentanil, 20 to 30 μg,[91] or fentanyl, 75 to 100 μg,[41, 71] during cesarean section under epidural anesthesia with 0.5% bupivacaine has been reported. Enhancement of comfort with a combination of lidocaine and fentanyl has also been shown to occur.[75] These combinations do not appear to produce any measureable effect on the neonate delivered by cesarean section. In another surgical setting, it has been shown that intrathecal morphine can attenuate lower extremity tourniquet pain sometimes observed under spinal anesthesia with hyperbaric bupivacaine.[89]

References

1. Abouleish EI: Epinephrine improves the quality of spinal hyperbaric bupivacaine for cesarean section. Anesth Analg 66:395–400, 1987
2. Albright GA, Jouppila R, Hollmen A, et al: Epinephrine does not alter human intervillous blood flow during epidural anesthesia. Anesthesiology 54:131–135, 1981
3. Appleyard TN, Witt A, Alkinson RE, et al: Bupivacaine carbonate and bupivacaine hydrochloride: A comparison of blood concentrations during epidural blockade for vaginal surgery. Br J Anaesth 46:530–533, 1974
4. Bannister J, McClure JH, Wildsmith JAW: Effect of glucose concentration on the intrathecal spread of 0.5% bupivacaine. Br J Anaesth 64:232–234, 1990
5. Bedder MD, Kozody R, Palahniuk RJ, et al: Clonidine prolongs canine tetracaine spinal anesthesia. Can Anaesth Soc J 33:591–596, 1986
6. Benhamou D, Labaille T, Bonhomme L, et al: Alkalinization of epidural 0.5% bupivacaine for cesarean section. Reg Anesth 14:240–243, 1989
7. Bonhomme L, Benhamou D, Jebri M, et al: Chemical stability of bupivacaine in pH-adjusted solutions. Anesthesiology 69:754–756, 1988
8. Bonica JJ, Backup PH, Pratt WH: The use of vasoconstrictors to prolong spinal anesthesia. Anesthesiology 12:431–440, 1951
9. Bonnet F, Brun-Buisson V, Saada M, et al: Dose-related prolongation of hyperbaric tetracaine spinal anesthesia by clonidine in humans. Anesth Analg 68:619–622, 1989
10. Braun H: Local anesthesia. Its scientific basis and practical use, ed 3. Philadelphia, Lea & Febiger, 1914
11. Braun H: Ueber den Einfluss der Vitalitat der Gewebe auf die ortlichen und allgemeinen Giftwirkungen localanasthesirender Mittle und uber die Bedeutung des Adrenalins fur die Localanasthesie. Arch Klin Chir 69:541, 1903
12. Bromage PR, Burfoot MF, Crowell DE, et al: Quality of epidural blockade III: Carbonated local anesthetic solutions. Br J Anaesth 39:197–208, 1967
13. Bromage PR, Comporesi EM, Nielson CH, et al: The effects of epinephrine as an adjuvant to epidural morphine. Anesthesiology 57:A195, 1982
14. Bromage PR, Gertel M: Improved brachial plexus blockade with bupivacaine hydrochloride and carbonated lidocaine. Anesthesiology 36:479–481, 1972
15. Bromage PR: A comparison of the hydrochloride carbon dioxide salt of lidocaine and prilocaine in epidural anesthesia. Acta Anaesthesiol Scand 55 (suppl XVI):55–69, 1965

16. Bromage PR: Epidural Analgesia. Philadelphia, Saunders, 1978, pp 100–105, 299
17. Brown DT, Morrison DN, Covino BG, et al: Comparison of carbonated bupivacaine and bupivacaine hydrochloride for extradural anaesthesia. Br J Anaesth 52:419–422, 1980
18. Burfoot MF, Bromage PR: The effects of epinephrine on mepivacaine absorption from the spinal epidural space. Anesthesiology 35:488–492, 1971
19. Caldwell C, Nielsen C, Baltz T, et al: Comparison of high-dose epinephrine and phenylephrine in spinal anesthesia with tetracaine. Anesthesiology 62:804, 1985
20. Carpenter FG: Alterations in the stability of mammalian A fibres produced by N_2O and by CO_2. Am J Physiol 200:187, 1961
21. Carpenter FG: The stabilizing action of carbon dioxide on peripheral nerve fibres and on the neurons of the medullary reticular formation in the rat. Ann NY Acad Sci 109:480, 1963
22. Catchlove RFH: Potentiation of two different local anesthetics by carbon dioxide. Br J Anaesth 45:471–473, 1973
23. Catchlove RFH: The influence of CO_2 and pH on local anesthetic action. J Pharmacol Exp Ther 181:298–309, 1972
24. Chambers WA, Littlewood DG, Logan MR, et al: Effect of added epinephrine on spinal anesthesia with lidocaine. Anesth Analg 60:417–420, 1981
25. Chambers WA, Littlewood DG, Scott DB: Spinal anesthesia with hyperbaric bupivacaine: Effect of added vasoconstrictors. Anesth Analg 61:49, 1982
26. Chestnut DH, Weiner CP, Martin JG, et al: Effect of intravenous epinephrine on uterine artery blood flow velocity in the pregnant guinea pig. Anesthesiology 65:633–636, 1986
27. Concepcion M, Maddi R, Francis D, et al: Vasoconstrictors in spinal anesthesia with tetracaine—A comparison of epinephrine and phenylephrine. Anesth Analg 63:134–138, 1984
28. Condouris Ga, Shakalis A: Potentiation of the nerve-depressant effect of local anesthetics by carbon dioxide. Nature 204:57–59, 1964
29. Coombs DW, Saunders RL, Lachance D: Intrathecal morphine tolerance: use of intrathecal clonidine, DADLE, and intraventricular morphine. Anesthesiology 62:358–363, 1985
30. Crosby G, Russo M: The spinal blood flow effect of subarachnoid clonidine. Anesthesiology 67:A417, 1987
31. Denson DD, Bridenbaugh PO, Turner PA, et al: Neural blockade and pharmacokinetics following subarachnoid lidocaine in the Rhesus monkey. I. Effect of epinephrine. Anesth Analg 61:746–750, 1982
32. DiFazio CA, Carron H, Grosslight KR, et al: Comparison of pH-adjusted lidocaine solutions for epidural anesthesia. Anesth Analg 65:760–764, 1986
33. Egbert LD, Deas TC: Effects of epinephrine upon the duration of spinal anesthesia. Anesthesiology 21:345–347, 1960
34. Eisenach JC, Grice SC, Dewan DM: Epinephrine enhances analgesia produced by epidural bupivacaine during labor. Anesth Analg 66:447–451, 1987
35. Eisenach JC, Grice SC: Epidural clonidine does not decrease blood pressure or spinal cord blood flow in awake sheep. Anesthesiology 68:335–340, 1988
36. Eisenach JC, Lysak SZ, Viscomi CM: Epidural clonidine analgesia following surgery: Phase I. Anesthesiology 71:640–646, 1989
37. Eisenach JC, Rauch RL, Buzzanell C, et al: Epidural clonidine analgesia for intractable cancer pain: Phase I. Anesthesiology 71:647–652, 1989
38. Fink BR, Aasheim GM, Levy BA: Neural pharmacokinetics of epinephrine. Anesthesiology 48:263–266, 1978
39. Fleetwood-Walker SM, Mitchell R, Hope PJ, et al: An α_2 receptor mediates the selective inhibition by noradrenaline of nociceptive responses of identified dorsal horn neurons. Brain Res 334:243–254, 1985
40. Frazier DT, Narahashi T, Yamada M: The site of action and active form of local anesthetics. II. Experiments with quaternary compounds. J Pharmacol Exp Ther 171:45–51, 1969
41. Gaffud MP, Bansal P, Lawton C, et al: Surgical analgesia for cesarean delivery with epidural bupivacaine and fentanyl. Anesthesiology 65:331, 1986

42. Galindo A: pH-Adjusted local anesthetics: Clinical experience. Reg Anesth 8:35–36, 1983
43. Gordh T Jr, Feuk U, Norlen K: Effect of epidural clonidine on spinal cord blood flow and regional and central hemodynamics in pigs. Anesth Analg 65:1312–1318, 1986
44. Gordh T Jr, Post C, Olsson Y: Evaluation of the toxicity of subarachnoid clonidine, guanfacine, and a substance P-antagonist on rat spinal cord and nerve roots: Light and electron microscopic observations after chronic intrathecal administration. Anesth Analg 65:1303–1311, 1986
45. Guinard JP, Mulroy MF, Carpenter RL, et al: Test doses: Optimal epinephrine content with and without acute beta adrenergic blockade. Anesthesiology 73:386–392, 1990
46. Homeyer W, Mintz S, Adriani J: The effects upon the duration of spinal anesthesia of combining non-anesthetic substances with the agent. Anesthesiology 13:231, 1952
47. Hood DD, Dewan DM, James FM: Maternal and fetal effects of epinephrine in gravid ewes. Anesthesiology 64:610–613, 1986
48. Howie JE, Dutton DA: Epidural and Spinal Blockade in Obstetrics. London, Bailliere Tindall, 1990, pp 162–163
49. Ikuta PT, Raza SM, Durrani Z, et al: pH adjustment schedule for amide local anesthetics. Reg Anesth 14:229–235, 1989
50. Jouppila R, Jouppila P, Hollmen A, et al: Effect of segmental extradural analgesia on placental blood flow during normal labour. Br J Anaesth 50:563–567, 1978
51. Jouppila R, Jouppila P, Kuikka J, et al: Placental blood flow during caesarean section under lumbar extradural analgesia. Br J Anaesth 50:275–279, 1978
52. Kennedy WF, Bonica JJ, Ward RS, et al: Cardiorespiratory effects of epinephrine when used in regional anesthesia. Acta Anaesthesiol Scand 23(suppl):320–333, 1966
53. Kozody R, Swartz J, Palahniuk RJ, et al: Spinal cord blood flow following subarachnoid lidocaine. Can Anaesth Soc J 32:472–478, 1985
54. Krnjevic K, Randic M, Siesjo BK: Cortical CO_2 tension and neuronal excitability. J Physiol (Lond) 176:105, 1965
55. Laugner B, Muller A, Thiebaut JB: Analgesia with an implanted device for repetitive intrathecal injections of morphine. Ann Fr Anesth Reanim 4:511–520, 1985
56. Leicht CH, Carlson SA: Prolongation of lidocaine spinal anesthesia with epinephrine and phenylephrine. Anesth Analg 65:365–369, 1986
57. Littlewood DG, Buckley P, Covino BG, et al: Comparative study of various local anesthetic solutions in extradural block in labour. Br J Anaesth 51:47S–51S, 1979
58. Malinow AM, Mokriski BLK, Nomura MK, et al: Effect of epinephrine on intrathecal fentanyl analgesia in patients undergoing post partum tubal ligation. Anesthesiology 73:381–385, 1990
59. Martin R, Lamarche Y, Tetreault L: Comparison of the clinical effectiveness of lidocaine hydrocarbonate and lidocaine hydrochloride with and without epinephrine in epidural anaesthesia. Can Anaesth Soc J 28:217–223, 1981
60. Martin R, Lamarche Y, Tetreault L: Effects of carbon dioxide and epinephrine on serum levels of lidociane after epidural anaesthesia. Can Anaesth Soc J 28:224–227, 1981
61. McMorland GH, Douglas MJ, Jeffrey WK, et al: Effect of pH-adjustment of bupivacaine on onset and duration of epidural analgesia in parturients. Can Anaesth Soc J 33:537–551, 1986
62. Mehta P, Theriot E, Mehrotra D, et al: Shivering following epidural anesthesia in obstetrics. Reg Anesth 9:83–85, 1984
63. Mehta PM, Theriot E, Mehrotra D, et al: A simple technique to make bupivacaine a rapid-acting epidural anesthetic. Reg Anesth 12:135–138, 1987
64. Mensink FJ, Kozody R, Kehler CH, et al: Dose-response relationship of clonidine in tetracaine spinal anesthesia. Anesthesiology 67:717–721, 1987
65. Moore DC, Batra MS: The components of an effective test dose prior to epidural block. Anesthesiology 55:693–696, 1981

66. Moore DC, Chadwick HS, Ready LB: Epinephrine prolongs lidocaine spinal: Pain in the operative site only accurate method of determining duration of a local anesthetic. Anesthesiology 65:A194, 1986
67. Moore DC: Spinal anesthesia: Bupivacaine compared with tetracaine. Anesth Analg 59:743, 1980
68. Moore DC: The pH of local anesthetic solutions. Anesth Analg 60:833–834, 1981
69. Morison DH: A double-blind comparison of carbonated lidocaine and lidocaine hydrochloride in epidural anaesthesia. Can Anaesth Soc J 28:387–389, 1981
70. Narahashi T, Frazier DT, Yamada M: The site of action and active form of local anesthetics. I. Theory and pH experiments with tertiary compounds. J Pharmacol Exp Ther 171:32–44, 1969
71. Naulty JS, Datta S, Ostheimer GW, et al: Epidural fentanyl for postcesarean delivery pain management. Anesthesiology 63:694, 1985
72. Nickle PM, Bromage PR, Sherrill DL: Comparison of hydrochloride and carbonated salts of lidocaine for epidural analgesia. Reg Anesth 11:62–67, 1986
73. Ossipov MH, Suarez LJ, Spaulding TC: Antinociceptive interactions between α_2-adrenergic and opiate agonists at the spinal level in rodents. Anesth Analg 68:194–200, 1989
74. Porter SS, Albin MS, Watson WA, et al: Spinal cord and cerebral blood flow responses to subarachnoid injection of local anesthetics with and without epinephrine. Acta Anaesthesiol Scand 29:330–338, 1985
75. Preston PG, Rosen MA, Hughes SC, et al: Epidural anesthesia with fentanyl and lidocaine for cesarean section: Maternal effects and neonatal outcome. Anesthesiology 68:938, 1988
76. Racle JP, Benkhadra A, Poy JY, et al: Prolongation of isobaric bupivacaine spinal anesthesia with epinephrine and clonidine for hip surgery in the elderly. Anesth Analg 66:442–446, 1987
77. Racle JP, Poy JY, Benkhadra A, et al: Prolongation of spinal anesthesia with hyperbaric bupivacaine by adrénaline and clonidine in the elderly. Ann Fr Anesth Reanim 7:139–144, 1988
78. Rigler ML, Drasner K, Krejcie TC, et al: Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg 72:275–281, 1991
79. Ritchie JM, Greengard P: On the active structure of local anesthetics. J Pharmacol Exp Ther 133:241–245, 1961
80. Ritchie JM, Ritchie B, Greengard P: The active structure of local anesthetics. J Pharmacol Exp Ther 150:152–159, 1965
81. Ritchie JM, Ritchie B, Greengard P: The effect of the nerve sheath on the action of local anesthetics. J Pharmacol Exp Ther 150:160–164, 1965
82. Smith HS, Carpenter RL, Bridenbaugh LD: Failure rate of tetracaine spinal anesthesia with and without epinephrine. Anesthesiology 65:A193, 1986
83. Spivey DL: Epinephrine does not prolong lidocaine spinal anesthesia in term parturients. Anesth Analg 64:468–470, 1985
84. Stevens RA, Chester WL, Gruetter JA, et al: The effect of pH adjustment of 0.5% bupivacaine on the latency of epidural anesthesia. Reg Anesth 14:236–239, 1989
85. Strobel GE, Bianchi CP: The effect of pH gradients on the action of procaine and lidocaine in intact and desheathed sciatic nerves. J Pharmacol Exp Ther 172:1–17, 1970
86. Strobel GE, Bianchi CP: The effects of pH gradients on the uptake and distribution of C14-procaine and lidocaine in intact and desheathed sciatic nerve trunks. J Pharmacol Exp Ther 172:18–32, 1970
87. Sukhani R, Winnie AP: Clinical pharmacokinetics of carbonated local anesthetics II: Interscalene brachial block model. Anesth Analg 66:1245–1250, 1987
88. Tamsen A, Gordh T: Epidural clonidine produces analgesia. Lancet 2:231–232, 1984
89. Tuominen M, Valli H, Kalso E, et al: Efficacy of 0.3 mg morphine intrathecally in preventing tourniquet pain during spinal anesthesia with hyperbaric bupivacaine. Acta Anaesthesiol Scand 32:113–116, 1988
90. Vercauteren M, Lauwers E, Meert T, et al: Comparison of epidural sufentanil plus clonidine with sufentanil alone for postoperative pain relief. Anaesthesia 45:531–534, 1990

91. Vertommen JD, Vandermeulen E, Shnider SM, et al: The effect of the addition of epidural sufentanil to bupivacaine 0.5% for elective cesarean section. Abstracts of Scientific Papers. Presented at the Annual Meeting of the Society for Obstetric Anesthesia and Perinatology, D-12, 1989
92. Wallis KL, Shnider SM, Hicks JS, et al: Epidural anesthesia in the normotensive pregnant ewe. Anesthesiology 44:481–487, 1976

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BARICITY AND SPINAL ANESTHESIA: WHAT SOLUTION WHEN?

J. A. W. Wildsmith, MD, FC Anaes

The great attraction of spinal (subarachnoid) anesthesia is that very profound block to nerve conduction can be produced over large areas of the body with very small amounts of drug. The great challenge in clinical practice is to control the spread of that drug through the cerebrospinal fluid (CSF) so that the extent of block is adequate for the projected surgery, but not so widespread that the risk of complications is unnecessarily great. Ever since its first clinical use, practitioners of spinal anesthesia have been intrigued by what the method's pioneer, August Bier of Kiel, called the "lauenhaft,"[10] i.e., waywardness, or the variability between patients in either extent or duration of block that may be seen after technically identical injections. This, and to an even greater extent the toxicity of cocaine, discouraged Bier, and it was only when better drugs were available that this variability was investigated.

The first to examine the problem systematically was Arthur Barker, a surgeon at University College Hospital, London. He made models of the spinal canal from glass tubes and by injecting colored solutions was able to study the influence of various factors on spread. He concluded that in the supine position the "high" point of the canal was the third lumbar interspace and that there was a downslope from there to the fifth or sixth thoracic vertebra. Before Barker's model, it had been thought that the drug spread by diffusion or bulk displacement of CSF, but he deduced that gravity and the curves of the vertebral column could be used to influence the spread of solution, with a density different to that of CSF. As a result he devised a mixture (5% stovaine

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in 5% dextrose) that was hyperbaric and could be used with predictable effects.[7–9]

The opposite approach, using a solution that was less dense than CSF so that it would "float," was first employed by Babcock[5] in Philadelphia.[5] He worked at about the same time as Barker and also used stovaine, but dissolved it in an aqueous solution also containing alcohol and lactic acid. Again the interaction between gravity and the curves of the vertebral column was used to try and influence spread. The principles established by Barker and Babcock remain valid today and should be considered the cornerstones of spinal anesthetic practice. Many subsequent workers, notably Labat, Pitkin, and Etherington-Wilson, confirmed and extended their results, although sometimes not appreciating that they were simply repeating previous work.[20]

The main stimulus to such repeat experiments was often the production of a new local anesthetic drug. For instance, when tetracaine was introduced it was considered advantageous for spinal anesthesia because of its longer duration, but its effect was found to be variable, mainly because it was being used in a near isobaric solution. Tetracaine only became more predictable when Sise[41] applied Barker's technique and mixed it with 10% dextrose. The main impetus to the current interest in the factors influencing intrathecal drug spread was again almost certainly the introduction of a new drug—bupivacaine. History does keep repeating itself.

However, on this occasion other factors were also relevant, certainly in the United Kingdom. When concerns were expressed in the 1940s about the risk of neurologic complications of spinal anesthesia, the technique was virtually abandoned in favor of general anesthesia.[48] Because the vast majority of general anesthetics were given by a medical graduate other than the surgeon, a high standard was available. Thus, it was thought that the developments in general anesthesia would allow all the problems to be avoided and that the risk of paraplegia after a spinal anesthetic was unacceptable. After 30 years it was recognized that there were still unsolved problems with general anesthesia, and spinal (and other forms of regional blockade as well) began to be used again, but by a whole generation of practitioners without preconceived notions. Thus, it was investigated almost as if it was an entirely new method.

The question of preconceived notions was relevant in other countries also because bupivacaine was the first significant local anesthetic drug to be developed after the establishment of anesthesiology as an independent specialty with a significant academic component. The great majority, if not all, of the early pioneers of spinal anesthesia were surgeons, and they had developed very didactic approaches, typified by Pitkin's review of 1928.[36] Precise, and perhaps rather complicated, recommendations were made about baricity of solution, patient posture, level of injection, and dose and volume of solution that were to be employed to produce a block of a particular distribution.

Clearly these methods worked in the individual situation or they would have been abandoned by their advocates, but that did not make them universally applicable. The anesthetists of the time rarely had a chance to test the theories because the right to perform the blocks was often jealously guarded by the surgeons. Barker was doubtful of the technique "drifting into the hands of the professional anaesthetists,"[8] who Jonnesco (another surgical pioneer of spinal anesthesia) considered "often inexperienced, never responsible."[1] When bupivacaine began to be used intrathecally, this was no longer the case and old concepts were challenged.

INTRATHECAL DRUG SPREAD

Spinal anesthesia is normally performed by puncture of the dura and arachnoid mater in the lumbar region, and local anesthetic is introduced directly into the CSF surrounding the nerve roots and spinal cord. The solution spreads longitudinally and the drug is taken up by the neuronal tissue that it reaches. Whether an effective concentration results in a particular nerve depends on its accessibility, lipid content, and blood flow.[21] The nerve roots of the cauda equina are easily accessible and exposed over a considerable surface, but this may not be the case with more cephalad roots.

Thus, the most important determinants of a spinal anesthetic are the factors that affect spread of solution through the CSF. Greene[22] has enumerated 25 of these and recent controlled clinical trials, using loss of sensation to pinprick to define spread, have indicated the clinically important factors. This work may be summarized in the following sections.

Definitions

A number of terms (density, specific gravity, and baricity) are used, somewhat loosely and interchangeably, to describe the characteristics of spinal anesthetic solutions. In fact, each has a very precise definition.

The *density* of a substance is the ratio of its mass to its volume and obviously varies with temperature. The *specific gravity* is the ratio of the density of the substance compared with a standard. The temperature of both must be specified, and it is usual to relate local anesthetic solutions at 20°C to water at 4°C. *Baricity* is analagous to specific gravity, but the ratio is between the densities of local anesthetic solution and CSF, both at 37°C. The dimensions of density are weight per unit volume, but the other two parameters are dimensionless. Table 1 gives the various figures for a number of agents. The most relevant number is obviously the baricity because this indicates how the solution will "behave" after injection.

Solution Baricity

Using 1% tetracaine mixed with an equal volume of water, saline, or 10% dextrose, Brown and colleagues[11] found that baricity had a

Table 1. PHYSICAL CHARACTERISTICS OF SPINAL ANESTHETIC SOLUTIONS AT 37°C*

	Density	Specific Gravity	Baricity
Water	0.9934	1.0000	0.9931
CSF	1.0003	1.0069	1.0000
Tetracaine			
0.33% in water	0.9980	1.0046	0.9977
1.0% in water	1.0003	1.0007	1.0000
0.5% in 50% CSF	0.9998	1.0064	0.9995
0.5% in half normal saline	1.0000	1.0066	0.9997
0.5% in 5% dextrose	1.0136	1.0203	1.0133
Dibucaine			
0.066% in 0.5% saline	0.9970	1.0036	0.9976
Bupivacaine			
0.5% in water	0.9993	1.0059	0.9990
0.5% in 8% dextrose	1.0210	1.0278	1.0207
Procaine			
2.5% in water	0.9983	1.0052	0.9983
Lidocaine			
2% in water	1.0003	1.0066	1.0003
5% in 7.5% dextrose	1.0265	1.0333	1.0265

*Mean values.

From Greene NM: Distribution of local anesthetic solutions within the subarachnoid space. Anesth Analg 64:715, 1985; with permission.

major effect on the distribution of analgesia. The solution was injected at the third lumbar interspace in patients placed in the lateral horizontal position and turned supine immediately afterward. The hyperbaric solution resulted in a *mean* block to midthoracic level and the isobaric solution to the level of the umbilicus. The hypobaric solution produced a mean level similar to the isobaric solution, but in comparison the blocks were patchy and sometimes of poor quality. It is of course more usual to use a larger volume of a more dilute solution for hypobaric spinal anesthesia, but the result discouraged these workers from using such solutions subsequently.

Dose of Drug

In the previously mentioned study of baricity, each of the solutions was injected in subgroups of patients in one of two doses: 10 or 15 mg. There were no differences in the extent of block produced by either of these two markedly different doses with any of the three solutions studied. Such a finding is contrary to much previous teaching, but was a very consistent result. What the study did show was that the rate of block regression was significantly slower in the patients who received the larger dose so that it did increase duration.

Patient Posture

Posture has been used since the time of Barker's classic descriptions to aid or restrict the spread of injected solution. If a patient is turned supine immediately after injection at the third or fourth lumbar interspace, the solution will, as he pointed out, be at the apex of the lumbar spinal curve. As a result gravity causes a hyperbaric solution to spread down from the apex in both sacral and thoracic directions. Thus, with a hyperbaric solution it is not necessary to use Trendelenburg's position to ensure spread to the midthoracic level.

Sinclair and colleagues,[40] using hyperbaric bupivacaine, found that all that this maneuver did was to increase the variability of the height of the block and thus increase the incidence of blocks extending into the cervical region. Accentuation of the lumbar curve in pregnancy may explain in part the increased spread seen when spinal anesthesia is performed with a hyperbaric solution for cesarean section. Conversely, flexion of the hips in the supine position flattens the lumbar curve and has been shown to decrease the spread of hyperbaric solutions.[43]

A major reason for the use of posture to control the spread of hyperbaric solutions is to try and restrict spread to the lower limbs and perineum. Wildsmith and colleagues[49] investigated the effect of maintaining both the lateral and sitting positions for 5 minutes after the injection of hyperbaric or isobaric solutions of tetracaine. They concluded that if posture is to be used to control the spread of a hyperbaric solution, then the particular position must be maintained for considerably longer than is often the case. Even when patients were sitting for 5 minutes, spread above the level of injection was seen in more than half the patients given a hyperbaric solution, and maintenance of the lateral position for the same period of time had very little ultimate effect because the block spread to the other side after the patient was turned supine. This study also found that posture had no effect at all on the spread of a truly isobaric solution and concluded that such a solution has much to commend it when the aim is to produce a block limited to the legs and perineum.

Volume and Rate of Injection

Increasing the dose of a spinal anesthetic injection usually increases the volume of solution injected as well, so a study was devised in which a standard dose of tetracaine was dissolved in 1, 2, or 4 mL of an isobaric solution of normal saline.[27] There was very little difference in mean spread with the different volumes, but the larger the volume injected, the greater was the range of blocks, i.e., predictability was reduced. Slowing the rate of injection of 4 mL reduced the range of blocks and made the solution more predictable again. It was concluded that the most predictable spinal blocks might be obtained by using a low volume solution at a slow rate, given consistency in the other features of the injectate.

Level of Injection

It is quite obvious that the level of injection has some effect on the ultimate height of the block. With plain solutions this effect is fairly predictable, and an increase in the level of injection by only one interspace (from the third to the second lumbar) has been shown to produce a significantly higher level of mean block.[26] Interestingly, a decrease in the level of injection from the third to the fourth lumbar space not only produced a lower mean block, but one that varied less about that mean as well.[45] The implication is that the lumbar CSF collection "buffers" the spread of the solution.

The effect of variation in level of injection has not been studied as systematically in recent times with solutions that differ markedly from CSF in density. Clinical experience suggests that injection of a nonisobaric solution at a space other than the third lumbar can, in fact, produce rather unusual blocks. When injected at that level, a hyperbaric solution, in the supine patient, spreads with gravity in both caudad and cephalad directions. However, with a lower or higher injection (or in a patient with an abnormal lordosis) the solution may only spread in either a caudad or a cephalad direction.

Patient Characteristics

Many anesthesiologists relate the dose of local anesthetic that they use for a spinal to the patient's height or weight. Although restricted spread is sometimes seen in the very thin patient, and the opposite in the obese, many studies have found that spread correlates very poorly with patient size, certainly within the adult range. For instance, McCulloch and Littlewood[29] have shown that there is some increase in spread in the obese patient, but that the overall range of blocks is so wide that this is of very little predictive help. The level of block was totally unrelated to patient height. Similarly, some correlation has been shown between patient age and intrathecal spread,[12, 35] but again the range of blocks seen in any particular age group is too wide for the information to be of any practical help. More recently it has been found that the effect of obesity on mean spread is relevant at different levels of injection.[46]

Effect of Clinical Interactions

The results of the studies outlined previously have indicated how the major factors affect the spread of local anesthetic solution after intrathecal injection. However, it is important to appreciate that these studies were performed in healthy patients under very carefully controlled conditions. In the routine clinical situation, variations in technique, differences in solution composition, and individual patient factors (e.g., distortion of the spine with age) may individually or together result in more variable spread.

For instance, Axelsson and colleagues[4] studied the spread of plain 0.5% bupivacaine (a slightly hypobaric solution) in patients who were sitting for 2 minutes after injection and then placed in the lithotomy position. They found that cephalad spread was proportional to the logarithm of the volume injected. Again, Chambers and his colleagues[16] found that volume had no effect on the spread of hyperbaric 0.5% bupivacaine, but that there was an effect on the spread of hyperbaric 0.75% bupivacaine. Others have in fact demonstrated some relationship between volume injected and the spread of hyperbaric 0.5% bupivacaine.[3, 44]

Such contradictory results may be due to a number of factors, including simple chance. It is important to remember the opening premise that any technique of spinal anesthesia results in a range of blocks, even when it is applied consistently by a single practitioner. Therefore, it is not surprising that there should be some variation between the results of studies in which there may be subtle, seemingly irrelevant variations in technique, drug composition, and patient characteristics. Too many investigators have not appreciated the importance of keeping every factor completely constant, except the one being studied.

This point was clearly appreciated by Olsen and colleagues[34] when interpreting the results of their study, which did *not* find a statistically significant difference in the effects of injecting plain bupivacaine at either the second or third lumbar interspace. The protocol involved injection in the sitting position, which was maintained for 2 minutes, after which the patients were laid supine for 5 minutes before being placed in the lithotomy position. Other studies of level of injection were performed in the lateral position and the patients placed supine thereafter.[26] Since all these workers used plain bupivacaine, which is slightly hypobaric, it reconfirms that baricity is the overriding factor influencing intrathecal drug spread. Although the evidence is clear that we cannot use gravity to control spread as accurately as we would like, it still has the most important influence if the solution has a density different from that of CSF.

Minor Differences in Baricity

This confirmation that baricity is the most important factor, coupled with the realization that manipulation of the other factors tended to influence only the variability of blocks in any particular group of patients,[28] has led to some workers investigating the influence of differences in baricity that are smaller than is conventional. Lee and colleagues[25] compared 0.5% solutions of tetracaine containing 0%, 1.25%, 2.5%, and 5% dextrose after injection into supine subjects. All the dextrose solutions produced blocks to the midthoracic level, although the initial rate of spread of the 1.25% dextrose solution was slightly slower.[25]

This encouraged the same group to examine the spread of solutions containing even lower concentrations of dextrose, this time using 0.5% bupivacaine. This drug was chosen because its plain solution causes very variable blocks and its hyperbaric solution (containing 8% dextrose) very extensive ones. The study showed that 0.83% dextrose (a concentration that results in a density only marginally greater than that of CSF) produced a guaranteed block to the level of the umbilicus, but with little chance of spread to the upper thoracic segments.[6] This is a very promising result, but clearly it requires confirmation.

An alternative approach to achieving the same end was tried by Kristoffersen and colleagues.[23] They injected plain 0.5% bupivacaine at either 19°C or 37°C, the increase in temperature making the solution less dense, a change that in sitting patients (2 minutes in the study) might be expected to make the solution rise further, but the effect was in fact only minor and of little clinical significance. Taivainen and colleagues[46] made plain bupivacine even more hypobaric by diluting it from 0.5% to 0.19% with distilled water, but had to abandon their study, again in patients seated for 2 minutes, because of the occurrence of very extensive blocks. Of course, by diluting the solution they introduced a difference in volume, as well as baricity, between their groups, but a solution density much below that of CSF can only be achieved in that way unless solvents other than water are used.

FACTORS AFFECTING DURATION

The topic of this review, baricity, is obviously of importance in relation to its effect on the extent of block, but it will also affect duration. Thus, the other factors that influence duration also have to be considered because it is not enough to ensure that the block is extensive enough at the start of surgery. It has to last long enough at the level of surgery as well. Anxiety about this is the obvious reason for the long-standing popularity for spinal anesthesia of drugs from the longer acting group. However, it must be remembered that there are problems with a very prolonged block if the operation is of relatively short duration. The patient may find it unpleasant, and the need for close supervision is unnecessarily prolonged. The aim should be to tailor both the extent and the duration to the operation.

Studies investigating the duration of spinal blockade vary considerably in their definitions of duration, and this has made interpretation difficult.[15] In addition, the patient who has undergone an abdominal operation under spinal anesthesia has little interest in the duration of block in the feet, which in that situation is of little clinical relevance. Of course the reverse is true when the operation is performed on the feet. Whatever drug is considered, it is important to understand the pattern of offset of a spinal anesthetic. Having reached its maximum extent, the block, after a finite period of time, begins to regress. Thus, the upper segments are blocked for a shorter time than the lower, because duration relates simply to the distribution of drug in the CSF, and its concentration is greatest at the point of injection.

As in any other block, the main determinants of duration are the drug used[19, 30–32, 42] and the dose injected.[11, 16, 49] It is common practice to add vasoconstrictors to spinal anesthetic solutions. The assumption is that the efficacy and the duration will be increased because of delayed vascular absorption. Controlled studies have shown that little clinically significant prolongation of effect is produced by the addition of epinephrine to lidocaine, bupivacaine, or tetracaine.[2, 17, 18] Phenylephrine does produce a statistically significant prolongation in the duration of tetracaine, but a more marked effect may be produced simply by increasing the dose of local anesthetic injected.[11]

A final complicating factor is that there is great variation in the duration of block that is produced by a fixed dose of a single drug. Even when addition of a vasoconstrictor leads to a statistically significant prolongation of effect, the range of durations is wide and there is considerable overlap with the range of durations produced by the solution without one.[38] Thus, while knowing the mean duration that any drug will produce is not irrelevant, the more important information is the range of durations at the dermatomal level of the operation. This can then be related to the projected duration of the operation and a drug preparation selected with the appropriate dermatome/duration therapeutic window.

It is in the production of the apropriate window that solution baricity is important, although clearly the effects of the other factors outlined previously have to be borne in mind as well. When a standard dose of a particular drug is injected, a widespread block results in a lower concentration of drug in each of the nerves to which the solution has spread than in a restricted block. Thus, in supine patients an isobaric solution produces a longer duration of block in the legs and perineum than a hyperbaric one. Conversely, if the patients are kept sitting for a good while after injection of the hyperbaric solution, the block of the perineal nerves will be longer than that produced by the isobaric solution because the extent of block will be restricted.

DRUGS AND RECOMMENDATIONS

Virtually every local anesthetic that has been produced has been used for spinal anesthesia. Given solutions equipotent in concentration and of the same baricity, the only variation to be expected in clinical effect is in duration of action, although there is some evidence that there may be subtle differences. For instance, tetracaine is said to be associated with a greater incidence of tourniquet discomfort than bupivacaine.[39] Generally, clinical decisions depend on what is readily available and that is governed as much by commercial, as by scientific factors.

The ideal spinal anesthetic preparation should be isotonic with CSF and contain no preservatives. Solutions that are not isotonic or contain preservatives may (in vitro, at least) damage nerve fibers,[14, 37] which only acquire a protective layer of perineurium after passing through the dura mater.[47] The preparation should be in a form that enables the anesthetist to adjust its baricity (by adding water, saline, or dextrose) before use, but still produce a relatively small volume to inject. Tetracaine is available as a 1% (isobaric) solution and a crystalline preparation. Both meet these requirements.

Most other drugs specifically marketed for intrathecal use, such as bupivacaine, are significantly hyperbaric, being presented in a solution containing greater than 5% dextrose, which also means that they are hypertonic. The plain solution of bupivacaine is used widely, but has two minor drawbacks. It is slightly hypobaric and has to be injected in relatively large volumes (3–4 mL) to ensure an adequate dose. The net effect is that plain bupivacaine, although producing the same mean spread as isobaric tetracaine in supine patients, produces a much wider range of blocks.[27, 35] As has been noted previously, it is an unpredictable solution and should be reserved for surgery of the perineum and distal part of the lower limbs because blocks extending no higher than the second lumbar dermatome are seen not infrequently.

If the patient is kept sitting for a short while after the administration of plain bupivacaine, its slight hypobaricity results in slightly higher blocks. Plain tetracaine (a truly isobaric solution) can be used with confidence for any procedure on the lower limb, yet has a much lower incidence of excessively high blocks than plain bupivacaine. An alternative strategy is to mix the plain and hyperbaric preparations of bupivacaine to produce a solution that is only slightly hyperbaric and behaves more predictably.[6]

Bupivacaine and tetracaine have one disadvantage in common—they are both relatively long-acting local anesthetics. Their durations may be manipulated to some extent by varying the dose, but for many procedures a shorter acting agent is better. A hyperbaric preparation of 5% lidocaine is available in many countries, and the plain solution of 2% lidocaine may be used also. Like plain bupivacaine, it produces a relatively wide range of blocks.[30]

The ultimate aim of all the clinical research into the factors affecting the extent and duration of an intrathecal injection of local anesthetic is to improve our control of the technique. The requirement is a block that is extensive and long lasting enough for the projected surgery, but does not extend too far above the level of the umbilicus and thus is unlikely to produce cardiorespiratory complications. The latter are perhaps more common if the block ascends to a high level in a short time. In young, healthy patients it might be argued that this does not matter too much and that the use of a standard hyperbaric preparation is all that is needed. However, unnecessarily extensive blockade was one relatively common feature in a series of patients who suffered cardiac arrest during spinal anesthesia.[13] In older patients, the need to limit block is all the more obvious.

Table 2. STRATEGIES FOR DIFFERENT LEVELS OF BLOCK

Level of Block	Perineum Only	Lower Limbs	Lower Abdomen	Upper Abdomen
Dextrose	5%	0	<1%	5%
Position	Sitting 5 min +	Any	Supine	Supine

See text for details.

Thus, strategies for producing different levels of block are required, and the author's practice, based on the research presented in this review, is summarized in Table 2. The fundamental principle is slow (0.2 mL $\sec^{-1}$) injection through a fine-bore needle (25 or 26 gauge) at the third lumbar interspace of a relatively low volume of solution, with baricity and posture being manipulated as shown. It is recognized that it is possible to take the many factors that influence intrathecal drug spread and manipulate them in other ways to produce similar effects. Perhaps the classical example would be the use of a hypobaric solution in the jackknife position to produce a saddle block. However, the approaches described here are relatively simple, involve minimal delay before surgery, and employ only solutions that are isotonic with CSF.

There is still concern about duration and, if single injection techniques are used, the anesthesiologist must balance the knowledge of how the particular dose of the chosen drug will perform against the knowledge of the surgeon's abilities. If there is any doubt about the likely duration of surgery, a single injection technique is contraindicated.

Recent developments in plastic technology have made available fine-bore catheters so that the advantages of intrathecal block can be available when the likely duration of surgery is not known. Continuous spinal anesthesia is reviewed elsewhere in this volume and does allow an entirely different approach. This accepts the variability inherent in intrathecal block and uses an incremental injection technique. Duration is certainly more controllable, but there is some evidence that a particular solution may not spread in just the same way as it would from a needle.[24, 33] The catheter introduces another variable to influence spread, and more studies are needed.

References

1. Annotation: Spinal anaesthesia. Lancet 2:1684–1685, 1909
2. Armstrong IR, Littlewood DG, Chambers WA: Spinal anaesthesia with tetracaine—Effect of added vasoconstrictors. Anesth Analg 62:793–795, 1983
3. Axelsson KH, Edstrom HH, Widman GB: Spinal anaesthesia with hyperbaric 0.5% bupivacaine—Effects of volume. Acta Anaesth Scand 26:439–445, 1982
4. Axelsson KH, Edstrom HH, Widman GB: Spinal anaesthesia with glucose free 0.5% bupivacaine—Effects of different volumes. Br J Anaesth 56:271–278, 1984
5. Babcock WW: Spinal anaesthesia: With report of surgical clinics. Surg Gynecol Obstet 15:606–622, 1912

6. Bannister J, McClure JH, Wildsmith JAW: Effect of glucose concentration on the intrathecal spread of 0.5% bupivacaine. Br J Anaesth 64:232–234, 1990
7. Barker AE: A report on clinical experiences with spinal analgesia in 100 cases. Br Med J 1:665–674, 1907
8. Barker AE: A second report on clinical experiences with spinal analgesia. Br Med J 1:244–249, 1908
9. Barker AE: A third report on clinical experiences with spinal analgesia. Br Med J 1:453–455, 1908
10. Bier AKG: Versuche iber cocainisierung des Rückenmarkes. Deutsche Zeitschrift für Chirurgie 51:361–369, 1899
11. Brown DT, Wildsmith JAW, Covino BG, et al: Effect of baricity on spinal anaesthesia with amethocaine. Br J Anaesth 52:589–596, 1980
12. Cameron AE, Arnold RW, Ghoris MW, et al: Spinal analgesia using bupivacaine 0.5% plain. Variations in the extent of block with patient age. Anaesthesia 36:318–322, 1981
13. Caplan RA, Posner K, Ward RJ, et al: Cardiac arrest during spinal anesthesia: A closed claims analysis of predisposing factors. Anesthesiology 68:5–11, 1988
14. Covino BG: Current controversies in local anaesthetics. *In* Scott DB, McClure JH, Wildsmith JAW (eds): Regional Anaesthesia 1884–1984. Sodertalje, Sweden, ICM, 1984, pp 74–81
15. Chambers WA: Intrathecal bupivacaine [editorial]. Br J Anaesth 54:799–801, 1982
16. Chambers WA, Littlewood DG, Edstrom HH, et al: Spinal anaesthesia with hyperbaric bupivacaine: Effects of concentration and volume administered. Br J Anaesth 54:75–80, 1982
17. Chambers WA, Littlewood DG, Logan MR, et al: Effect of added epinephrine on spinal anesthesia with lidocaine. Anesth Analg 60:417–420, 1981
18. Chambers WA, Littlewood DG, Scott DB: Spinal anesthesia with hyperbaric bupivacaine: Effect of added vasoconstrictors. Anesth Analg 61:49–52, 1982
19. Cummings GC, Bambes DB, Edstrom HH, et al: Subarachnoid blockade with bupivacaine. A comparison with cinchocaine. Br J Anaesth 56:573–579, 1984
20. Fink BR: History of neural blockade. *In* Cousins MJ, Bridenbaugh PO (eds): Neural Blockade in Clinical Anesthesia and Management of Pain, ed 2. Philadelphia, Lippincott, 1988, pp 3–21
21. Greene NM: Review: Uptake and elimination of local anesthetics during spinal anesthesia. Anesth Analog 62:1013–1024, 1983
22. Greene NM: Distribution of local anesthetic solutions within the subarachnoid space. Anesth Analg 64:715–730, 1985
23. Kristoffersen E, Sloth E, Husted JC, et al: Spinal anaesthesia with plain 0.5% bupivacaine at 19°C and 37°C. Br J Anaesth 65:504–507, 1990
24. Kestin IG, Goodman NW: Incremental spinal anaesthesia using a 32-gauge catheter. Anaesthesia 46:93–94, 1991
25. Lee A, Ray D, Littlewood DG, et al: Effect of dextrose concentration on the intrathecal spread of amethocaine. Br J Anaesth 61:135–138, 1988
26. Logan MR, McClure JH, Wildsmith JAW: Plain bupivacaine—An unpredictable spinal anaesthetic agent. Br J Anaesth 58:292–296, 1986
27. McClure JH, Brown DT, Wildsmith JAW: Effect of injected volume and speed of injection on the spread of spinal anaesthesia with isobaric amethocaine. Br J Anaesth 54:917–920, 1982
28. McClure JH, Wildsmith JAW: Aspects of spinal anaesthesia. *In* Kaufman L (ed): Anaesthesia Review 5. London, Churchill Livingstone, 1988, pp 269–285
29. McCulloch WJD, Littlewood DG: Influence of obesity on spinal analgesia with isobaric 0.5% bupivacaine. Br J Anaesth 58:610–614, 1986
30. McKeown DW, Stewart K, Littlewood DG, et al: Spinal anesthesia with plain solutions of lidocaine 2% and bupivacaine 0.5%. Reg Anesth 11:68–71, 1986
31. Marstrand T, Sorensen M, Andersen S: Spinal anaesthesia with 0.75% bupivacaine and 0.5% amethocaine in 5% glucose. Br J Anaesth 57:971–975, 1985
32. Moore DC: Spinal anesthesia: Bupivacaine compared with tetracaine. Anesth Analg 59:743–750, 1980
33. Morrison LMM, McClure JH, Wildsmith JAW: A clinical evaluation of a 24g spinal catheter in femoro-popliteal bypass grafting. Anaesthesia 46:576–578, 1991

34. Olsen KH, Nielsen TH, Kristoffersen E, et al: Spinal analgesia with plain 0.5% bupivacaine administered at spinal interspace L_{2-3} or L_{4-5}. Br J Anaesth 64:170–172, 1990
35. Pitkanen M, Haapaniemi L, Touminen M, et al: Influence of age on spinal anaesthesia with isobaric 0.5% bupivacaine. Br J Anaesth 56:279–284, 1984
36. Pitkin GP: Controllable spinal anesthesia. Am J Surg 5:537–553, 1928
37. Power I, Brown DT, Wildsmith JAW: The effect of fentanyl, meperidine and diamorphine on nerve conduction *in vitro*. Reg Anesth 16:204–208, 1991
38. Racle JP, Benkhadra A, Poy JY: Subarachnoid anaesthesia produced by hyperbaric lignocaine in elderly patients. Prolongation of effect with adrenaline. Br J Anaesth 60:831–835, 1988
39. Rocco AG, Concepcion MA, Sheskey MC, et al: A double-blind evaluation of intrathecal bupivacaine without glucose and a standard solution of hyperbaric tetracaine. Reg Anesth 9:1–7, 1984
40. Sinclair CJ, Scott DB, Edstrom HH: Effect of the Trendelenberg position on spinal anaesthesia with hyperbaric bupivacaine. Br J Anaesth 54:497–500, 1982
41. Sise LF: Pontocaine-glucose solution for spinal anesthesia. Surg Clin North Am 15:1501–1511, 1935
42. Skretting P, Vaagenes P, Sundnes KO, et al: Subarachnoid anaesthesia: Comparison of hyperbaric solutions of bupivacaine and amethocaine. Br J Anaesth 56:155–159, 1984
43. Smith TC: The lumbar spine and subarachnoid block. Anesthesiology 29:60–64, 1968
44. Sundnes KO, Vaagenes P, Skretting P, et al: Spinal anaesthesia with hyperbaric bupivacaine. Effects of volume of solution. Br J Anaesth 54:69–74, 1982
45. Taivanen T, Tuominen M, Rosenberg PH: Influence of obesity on the spread of spinal analgesia after injection of plain 0.5% bupivacaine at the L_{3-4} or L_{4-5} interspace. Br J Anaesth 64:542–546, 1990
46. Taivainen T, Tuominen M, Rosenberg PH: Spinal anaesthesia with hypobaric 0.19% or plain 0.5% bupivacaine. Br J Anaesth 65:234–236, 1990
47. Wildsmith JAW: Peripheral nerve and local anaesthetic drugs. Br J Anaesth 58:692–700, 1986
48. Wildsmith JAW, Lee JA: Neurological sequelae of spinal anaesthesia [editorial]. Br J Anaesth 63:505–507, 1989
49. Wildsmith JAW, McClure JH, Brown DT, et al: Effects of posture on the spread of isobaric and hyperbaric amethocaine. Br J Anaesth 53:273–278, 1981

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EPIDURAL TEST DOSES

Michael F. Mulroy, MD

The common serious risks of epidural anesthesia are unintentional subarachnoid or intravascular injection of a large volume of local anesthetic. The incidence of intravascular injection has been variously described as ranging between 2% and 10% during epidural blockade,[11, 16, 24] with the highest incidence occurring when epidural catheters are inserted before the local anesthetic is administered in pregnant women.[22, 41] Before 1980, the "standard" test dose was usually a 3-mL volume of the anesthetic solution planned for the epidural itself, because that quantity contained enough local anesthetic to produce spinal anesthesia if an unrecognized subarachnoid placement had occurred.[3] Intravascular placement was appraised by the presence of subjective symptoms produced by the local anesthetic. The quantity of drug in the 3-mL volume was never documented to produce reliable signs of intravascular injection. Interest in a reliable test dose to detect unintentional intravascular needle or catheter placement was rekindled around 1980, following the reports of cardiac arrests and difficult resuscitation after intravascular injections of large quantities of bupivacaine or etidocaine.[4, 29] With the suspected higher cardiac toxicity of these long-acting amide local anesthetics, a better means of prevention of systemic injection was sought.

STANDARD TEST DOSE

Moore and Batra[31] described the objective cardiovascular effects of 15 μg of epinephrine, a standard test dose, when injected intravascularly in normal patients. They reported on 175 surgical patients, who

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each received deliberate intravenous injections of 15 μg of epinephrine mixed with one of several local anesthetics suitable to test for subarachnoid injection. In all but three of these patients (see following), the pulse rate increased unmistakably in the first 60 seconds after injection. The average heart rate increased from 80 to 110 beats per minute, with the initial increase occurring at 20 seconds and the heart rate returning toward normal by 60 seconds (Fig. 1). They studied the 15-μg dose because that was the quantity of epinephrine contained in 3 mL of a 1:200,000 solution. They were the first to record objectively the cardiovascular changes and to show that the increase in heart rate was a reliable sign in normal patients.

They stressed the need for objective recording of heart rate with an electrical beat-to-beat counter. Subjective signs were solicited in their patients, who all received diazepam and fentanyl sedation. When questioned, only 56 of their patients (32%) reported the subjective sensation of palpitations. The rest responded that they felt sleepy. In their situation, subjective reporting of cardiac symptoms in premedicated subjects was unreliable. Their data also show that the pulse changes are evanescent. The traditional technique of counting the pulse for 15 seconds is not likely to be reliable in detecting changes that last less than a minute. A beat-to-beat calculation of rate is essential.

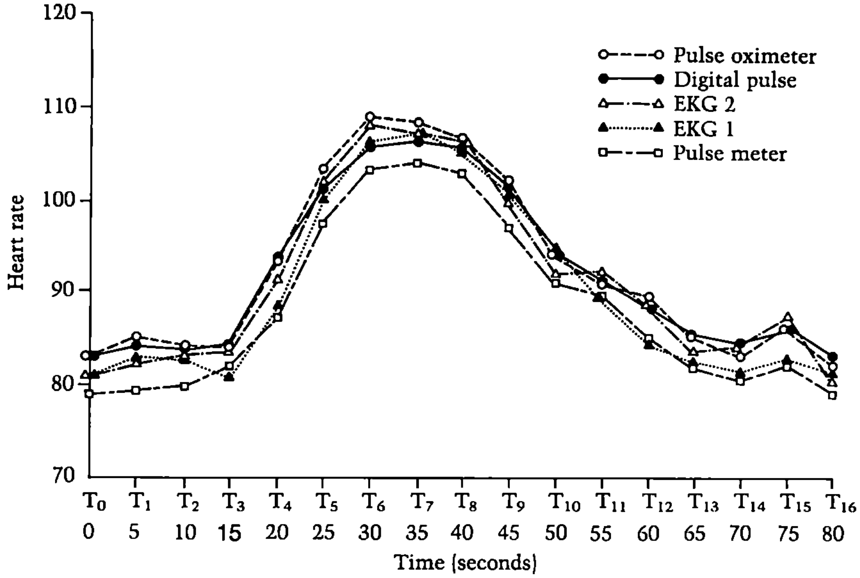

Figure 1. Typical average pulse rate changes in five normal subjects as measured with pulse oximeter, EKG, or plethysmograph pulse counters after intravenous injection of 15 μg of epinephrine at time zero. (*From* Mulroy M: Regional Anesthesia: An Illustrated Procedure Guide. Boston, Little Brown, 1989, p 107; with permission.)

PROBLEMS WITH TEST DOSES

A few problems have arisen since this report was published. First of all, they identified three patients who were being treated with beta-blockers. These did not respond to epinephrine injection with an increase in heart rate. Subsequent reports have raised a second issue: laboring pregnant women have extremely variable heart rates and may not have reliable changes following epinephrine injection. Epinephrine has also been alleged to compromise the progress of labor and uterine blood supply. Third, reduced sensitivity to catecholamines in elderly patients and pediatric patients under general anesthesia has been reported, and therefore, some of these patients may not produce reliable responses to epinephrine injection.

β-Blockade

In addition to the experience of Moore and Batra, isolated case reports have suggested that β-blockade interferes with epinephrine testing.[33, 38] Guinard et al[17] have confirmed that the presence of acute β-blockade with either a specific (β_1) or a nonspecific β-blocker (esmolol or propranolol) makes the heart rate change an unreliable indicator of intravascular injection of epinephrine. In a group of nine healthy young subjects, they observed that a change in heart rate of 20 beats per minute was a reliable sign of epinephrine injection with 10 or 15 μg, but that neither dose reliably produced a 20-beat-per-minute change in the presence of acute intravenous β-blockade. In fact, propranolol blockade actually resulted in a bradycardia after epinephrine, probably secondary to transient hypertension produced by unopposed α-adrenergic effect of epinephrine (Fig. 2). Preliminary study in our institution has shown that patients receiving chronic oral β-blockade do not demonstrate bradycardia even though they do have transient systolic hypertension. Further data are needed to document the response of larger populations taking chronic oral β-blockade therapy.

The systolic blood pressure did increase consistently, by 15 mm Hg, in the presence of both specific and nonspecific β-blockade. This may be the only reliable indicator of intravascular injection in this population. Unfortunately, the increase in blood pressure is also a transient phenomena, returning to baseline levels within 2 minutes. Johnson et al[21] reported that a standard automated noninvasive oscillometric blood pressure cuff may not reliably detect this transient phenomena. This may be due to internal mechanics of some of the machines, which will not record pressures at a heart rate below 45, or to other technical problems that prevent the machine from determining pressure in the presence of rapid changes. Guinard used the Finapres finger plethysmograph to record blood pressures. This device is not widely available. Frequent manual blood pressure determinations with a sphygmomanometer may be required in order to detect the changes

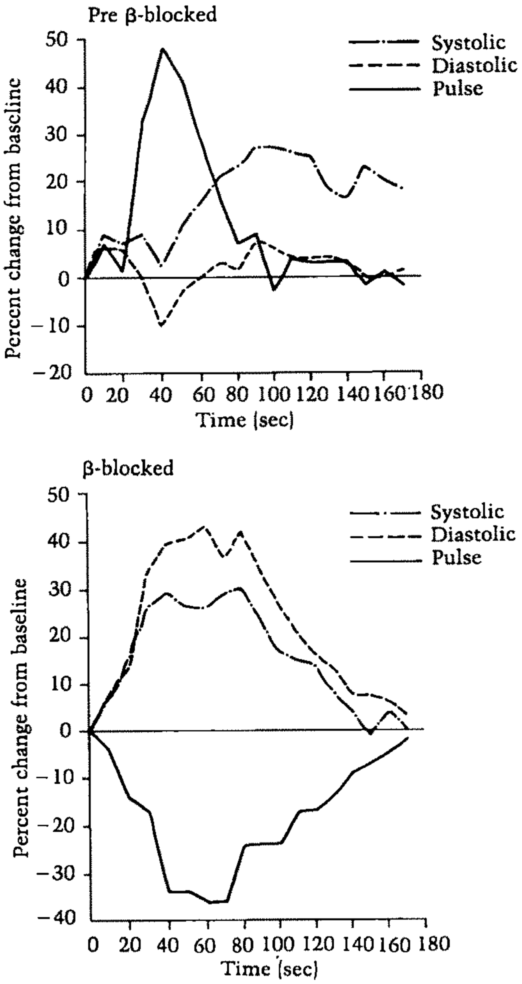

Figure 2. Heart rate and blood pressure changes (as a percentage change from baseline) in six normal subjects before and after beta blockade. In normal subjects, systolic blood pressure rises 20% above control; this rise follows the classic pulse rate change. After receiving propranolol, healthy young subjects will show an initial rise of systolic blood pressure and a reflex bradycardia. (*From* Hom M, Johnson PW, Mulroy MF: Blood pressure response to an epinephrine test dose in β-blocked subjects. Anesthesiology 67:A268, 1987; with permission.)

in β-blocked patients. A high level of suspicion and incremental injections are certainly appropriate under these circumstances.

Guinard did not report on the subjective responses to the epinephrine test dose in his subjects. It would be expected that most unpremedicated subjects would be able to appreciate and report the palpitations or increased systolic pressure associated with this test. Further study is required to document this assumption. Based on the previous experience of Moore and Batra, these subjective signs cannot be relied on in medicated subjects.

The Pregnant Patient

Recent controversy addresses the appropriateness of epinephrine test doses in pregnant patients. There are two concerns. One is that the maternal heart rate is sufficiently variable during labor that changes produced by epinephrine may be indistinguishable from the normal variations. Cartwright et al[6] studied a group of 100 laboring women and found that 24 had heart rate increases greater than 20 beats per minute and 12 had increases greater than 30 beats per minute following injection of a test dose that contained bupivacaine but no epinephrine. This would give a 12% false-positive rate if 30 beats per minute were chosen as the criterion for positivity; this would increase to 24% if the 20 beats per minute criterion of Guinard were employed. Fourteen women had contractions during the test period and had dramatic heart rate changes. They concluded that "the interpretation of the epinephrine test dose for obstetric anesthesia is difficult because of the poor specificity of the test." Chestnut et al[8] reported a similar experience, showing that five of ten normal patients in labor in their study had spontaneous increases of heart rate of more than 25 beats per minute during a 15-minute observation period before and after injection of a test dose. Four of the five had increases within 2 minutes of injection of the test dose, but none of the catheters were intravascular, as demonstrated by subsequent injection of effective analgesic doses.[8] Leighton et al[28] also have shown that the heart rate variability associated with labor makes the current regimen inaccurate. They injected 15 μg of epinephrine intravenously in ten laboring subjects, and could identify only five as responding positively based on an increase of 30 beats per minute from baseline.[28] Although they were able to obtain a higher degree of reliability using a more complicated "peak-to-peak" analysis of heart rate changes (Fig. 3), this technique is cumbersome and still not 100% effective. Even with peak-to-peak calculations, they could identify only nine out of ten epinephrine injections. Thus, the presence of labor may significantly interfere with the specificity of the standard test dose.

A second concern is that the presence of epinephrine may have adverse effects on the mother or the fetus by producing a reduction in uterine blood flow or of uterine contractions. In animal models, epinephrine infusion has been shown to reduce uterine artery blood flow in the guinea pig[9] and produce deleterious effects in the pregnant sheep fetus.[20] More significantly, the study by Leighton et al[28] identified two of ten patients who developed signs of fetal distress (one with bradycardia, one with late decelerations) following intravenous epinephrine injection. Further, there is concern about the possibility of unintentional intravascular epinephrine injection exacerbating the hypertension associated with preeclampsia.[44] Other experimental data do not support these concerns. Heller and Goodman[19] have reported the safe use of epinephrine-containing solutions in four preeclamptic patients, although none of these involved intravascular injections. Youngstrom et al[43] have reported that the bolus injection of 16.5 μg of epinephrine does not produce distress in the acidotic fetus in an anesthetized pregnant sheep model. This may be related to the transient elevation of blood levels produced by the bolus injection. This absence of changes in the stressed/acidotic sheep model is in contrast to the concerns raised by the report by Hood in normal sheep and fetuses,

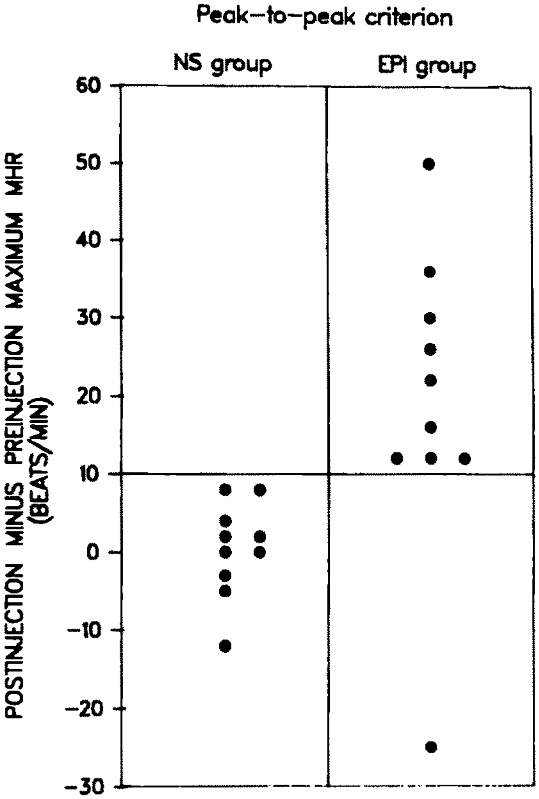

Figure 3 *(Continued).* The peak-to-peak criterion involves an increase of greater than 10 beats per minute in the maximum HR in the 2 minutes after injection compared with the highest HR in the 2-minute period before injection. Even this criterion only identified 9 of the 10 test injections. (*From* Leighton BL, Norris MC, Sosis M, et al: Limitations of epinephrine as a marker of intravascular injection in laboring women. Anesthesiology 66:688, 1987; with permission.) EPI = epinephrine; NS = not significant; HR = heart rate.

and even reduces the incidence of maternal hypotension. Albright[5] continues to recommend the use of the standard test dose, emphasizing the significant risks of unrecognized intravascular injection. Marx[29] supports the continued use of test doses, especially if bupivacaine is used. Van Zundert et al[39] recommend a modified test containing 12.5 mg of bupivacaine with 12.5 μg of epinephrine and report two anecdotal cases to support the reliability of this test. Like Chestnut and Weiner,[10] they advocate the use of a continuous electronic maternal heart monitor by using the standard fetal heart rate monitor device present in most labor suites.

There is continued interest in developing a safer, reliable, alternative test dose in obstetrics (see following). At the current time, the status of test doses in obstetric anesthesia might appear as follows:

1. In the patient presenting for elective cesarean delivery who is not in active labor, epinephrine is an apparently safe and reliable marker.
2. For pregnant women in labor, epinephrine may not be a reliable marker. Fortunately, the anesthetic requirements are small. Adequate analgesia can be obtained with as little as 3.5 mg of bupivacaine when this drug is used in a 0.0625% concentration combined with fentanyl. Even if higher concentrations are used, such as 0.25% bupivacaine, the anesthetic can and should be administered in divided doses, each of which serves as its own test dose by relying on the development of subjective symptoms.[40] The separation of these small injections prevents accumulation of toxic blood levels if the injection is intravascular. For prolonged labor, a continuous infusion of the dilute concentrations provides uninterrupted analgesia, with total doses that are insufficient to produce systemic toxicity even if an indwelling catheter migrates intravascularly. Thus, epinephrine can be omitted in these situations of low doses and incremental or continuous infusion, without a significant risk of systemic toxicity.
3. The greatest challenge currently is to find an appropriate test dose for the pregnant woman in active labor who requires the large doses of local anesthetic necessary for cesarean delivery. Heart rate changes from epinephrine may not be reliable in the presence of contractions, but the local anesthetic doses represent a significant risk to the mother. Currently, if epinephrine is not used, the combination of aspiration and careful use of incremental injection is probably the best approach.

The Elderly Patient

A decrease in sensitivity to catecholamines has been identified in the elderly. Specifically, with isoproterenol there is a fivefold increase in the amount of drug required to produce a 25 beat-per-minute increase in heart rate between those at age 20 compared with those at age 70.[30, 42] Guinard et al[18] have reported that the responsiveness to an epinephrine test dose appears to decline with increasing age, and that the response to 10 μg of epinephrine (and perhaps to 15 μg) may be unreliable over the age of 60. During the period of Moore and Batra's original report, epidural anesthesia was performed primarily on patients under 60 years of age at the Virginia Mason Medical Center. Thus, their original report does not include data on patients over this age, and further study is clearly warranted before the reliability of this test can be assumed in the elderly.

Anesthetized Patients

Desparmet et al[13] reported that 29% of a group of pediatric patients anesthetized with halothane did not respond to an epinephrine-containing test dose during surgery. It is not surprising that general anesthetics would blunt the response to catecholamines because of their general depressant effects on the myocardium. This may become a more frequent question as epidural anesthesia is employed more often to provide postoperative narcotic analgesia, and more epidural catheters may be inserted in the operating room at the conclusion of general anesthesia. Further data are needed in this area, especially for adult patients.

ALTERNATIVE TEST DOSES

In view of these recent concerns, several alternative test doses have been recommended, particularly in the pregnant population.

Local Anesthetic

One of the oldest traditions is the use of local anesthetic drugs themselves, which do produce subjective signs of early toxicity when injected intravascularly. These signs include lightheadedness, ringing or buzzing in the ears, perioral tingling, abnormal taste, altered hearing, and virtually any other vague subjective change in sensorium, including drowsiness. The doses required are larger than the doses necessary to produce subarachnoid anesthesia, and thus the standard test dose is insufficient. Clinical trials of the injection of 100 mg of chloroprocaine,[15] 100 mg of lidocaine,[34] or 25 mg of bupivacaine[2] have shown these doses to be reliable indicators of intravascular injection in unmedicated volunteers. Obviously, these injections should follow a preliminary standard test dose to exclude subarachnoid injection, because these volumes produce unwanted high levels of spinal anesthesia if injected subarachnoid.

Standard premedication may interfere with subjective responses. Moore and Batra found that diazepam and fentanyl interfere with the subjective recognition of epinephrine responses. On theoretical grounds, benzodiazepines might be expected to alter the cerebral sensitivity to local anesthetics and reduce their sensitivity as indicators. Neal et al[32] have shown that, at least for the chloroprocaine and bupivacaine test doses, their reliability is abolished by the presence of premedication with fentanyl and midazolam.

Isoproterenol

The injection of 5 μg of isoproterenol has been advocated. Although the chronotropic sensitivity to isoproterenol is reduced somewhat in pregnancy,[12] Leighton et al[26] reported that 5 μg produced a significant increase in maternal heart rate (compared with a saline injection), but that the complicated peak-to-peak analysis of heart rate was required to detect the change reliably. The standard baseline-to-peak analysis and the use of subjective changes were not reliable. Although preliminary animal data suggest that isoproterenol may have a wider safety margin for the fetus, they acknowledge that "the safety and efficacy of epidural isoproterenol must be demonstrated."

Air

One milliliter of air injected into an epidural vein produces clearly audible changes in heart sounds monitored with a precordial Doppler stethoscope.[27] This test has been recommended because a Doppler is usually available in the labor room, and air is a readily available marker. There have been no deleterious effects of air injection when used to locate the epidural space, or in the small series reported where it was deliberately injected into catheters that were identified as being intravascular by other means. There remains some concern that even small bubbles may have the potential to cross a patent foramen ovale and produce systemic embolic lesions. The frequency of unsuspected patent foramen ovale in an adult population has been reported at 25%[23] and has been related to strokes in anesthetized and ambulatory patients. Paradoxical embolism has not been reported to occur even with the frequent identification of intravenous air embolism that has been reported during cesarean section. Nevertheless, this proposal needs further evidence supporting its clinical reliability and utility. A major problem is that the placement of a precordial Doppler is a fine art even in the operating room on anesthetized patients. Correct localization on the chest of a pregnant woman having contractions must represent some challenges that will increase the likelihood of a false-negative result.

Ephedrine

Fifteen milligrams of ephedrine has been shown to produce a reliable indication of intravascular injection,[7] but this detection again requires the complicated peak-to-peak methodology for analysis of systolic blood pressure changes. The alterations of pulse alone are not reliable. This makes clinical application difficult because of the need for a long baseline analysis and careful determinations of blood pressures. Although Cherala and Greene[7] found this technique adequate, others have not found it useful.[14]

Even though preliminary studies have indicated that these latter three techniques may be reliable, they are not practical for most anesthesiologists performing epidural anesthesia because of the requirement for special drugs, equipment, or analysis of data. Likewise, other suggestions, such as injection of dyes that could be detected by the pulse oximeter, have not proved practical or popular.[37] Further study is needed before any alternative marker of intravascular injection can be accepted to replace the current epinephrine standard. Even though there are reports of false-negative results with the current regimen,[25, 35] it seems prudent to include 15 μg of epinephrine as a part of our standard test procedure (along with careful aspiration and incremental injection[36, 40]) until a better alternative is found.

Subarachnoid Test Solutions

The other risk of epidural injection is an unintentional subarachnoid placement that produces a high or total spinal anesthetic. As mentioned, the original test doses were designed to prevent this, since a 3-mL volume usually contains sufficient local anesthetic to produce early blockade, which can be distinguished from epidural anesthesia. It is critical to evaluate this test adequately. Abraham et al[3] have shown that 1.5% hyperbaric lidocaine (2 or 3 mL) produces sensory anesthesia after epidural injection, but not before 3 minutes. In contrast, the same drug injected subarachnoid produces sensory changes to pinprick in the S2 skin distribution with 2 minutes (Fig. 4). Thus, adequate testing requires specific evaluation of pinprick appreciation in the S2 dermatome at 2

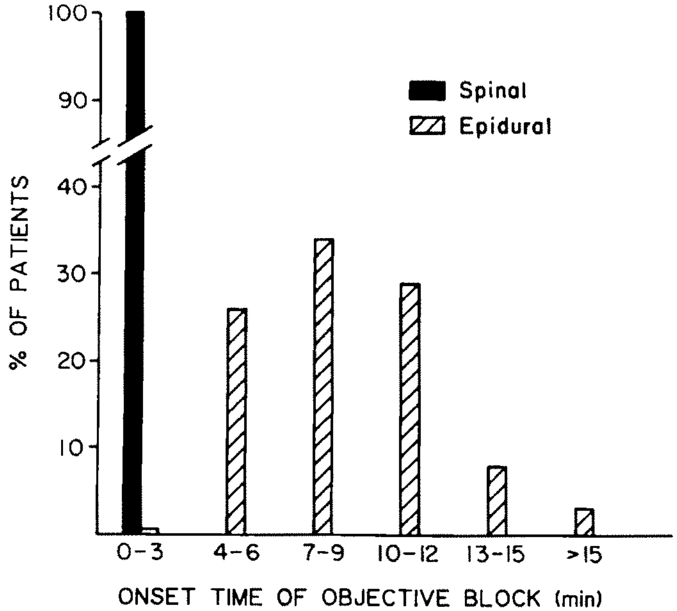

Figure 4. Time to onset of objective loss of pinprick sensation in the S2 dermatome following epidural or spinal anesthesia with 1.5% hyperbaric lidocaine. (*From* Abraham RA, Harris AP, Maxwell LG, et al: The efficacy of 1.5% lidocaine with 7.5% dextrose and epinephrine as an epidural test dose for obstetrics. Anesthesiology 64:116, 1986; with permission.)

Table 1. CURRENT STANDARD TESTS FOR INTRAVASCULAR INJECTION

Situation	Epidural Test?	Procedure
Surgical patient	Yes	Careful aspiration; 15-μg epinephrine test dose with pulse monitor; incremental injection
Pregnant patient	Maybe	See text: elective cesarean-section; epidural labor
β-Blocked patient	Yes, but skeptically	Blood pressure monitoring
Elderly, anesthetized patient	Yes, but skeptically	Careful aspiration and incremental injections

minutes following injection. There are no good data available for other local anesthetics, such as bupivacaine, which might have a slower onset. When more drugs, other baricity, or more dilute concentrations are used, as in obstetrics, a longer time must be allowed, and specific attention paid to objective sensory changes. The custom of asking the patient to evaluate movement of the toes or legs is not valid in the early period after injection, and certainly not with the dilute concentrations that will not produce motor blockade. Other dermatomes may need to be tested if an isobaric of hypobaric solution is used.

Many anesthesiologists do not wait for a subarachnoid test dose, but rely on their clinical ability to appreciate fluid return through an 18- or 17-gauge needle. If there is any question, a specific test of sensory anesthesia as described is most appropriate.

SUMMARY

Despite these controversies, it is still safe to summarize the current procedure for safe epidural anesthesia. Appropriate safety steps including the following:

1. Careful aspiration before injection of a needle or catheter. This may require removal of bacterial filters or other obstructions to flow.
2. Use of an epinephrine-containing test dose, with 15 μg of epinephrine and (a) a mechanical or electrical pulse counter; (b) quiet, close observation following injection of the test dose: no conversation or other stimulus should be allowed to interfere with assessment of the patient response in the first 45 seconds following injection; and (c) repetition of the test if results are equivocal.
3. Assessment of sensory anesthesia in the S2 dermatome 2 minutes after injection, if subarachnoid placement is suspected.
4. Incremental injection of 5-mL boluses of anesthetic solution at 30-second intervals, with careful attention to patient mental status.

5. In any of the special situations described (Table 1), the procedure is modified appropriately.

As always, regional techniques must be performed in the setting of adequate resuscitation equipment and constant vigilance. None of the tests described will infallibly prevent intravascular or subarachnoid injection.

References

1. Abboud TK, Sheik-ol-Eslam A, Yanagi T, et al: Safety and efficacy of epinephrine added to bupivacaine for lumbar epidural analgesia in obstetrics. Anesth Analg 64:585–591, 1985
2. Abouleish E, Bourke D: Concerning the use and abuse of test doses for epidural anesthesia. Anesthesiology 61:344–345, 1984
3. Abraham RA, Harris AP, Maxwell LG, et al: The efficacy of 1.5% lidocaine with 7.5% dextrose and epinephrine as an epidural test dose for obstetrics. Anesthesiology 64:116, 1986
4. Albright GA: Cardiac arrest following regional anesthesia with etidiocaine or bupivacaine. Anesthesiology 51:285, 1979
5. Albright GA: Epinephrine should be used with the therapeutic dose of bupivacaine in obstetrics [letter]. Anesthesiology 61:217–218, 1984
6. Cartwright PD, McCarroll SM, Antzaka C: Maternal heart rate changes with a plain epidural test dose. Anesthesiology 65:226–228, 1986
7. Cherala SR, Greene R: Ephedrine as a marker of intravascular injection in laboring parturients. Reg Anesth 15:15, 1990
8. Chestnut DH, Owen CL, Brown CK, et al: Does labor affect the variability of maternal heart rate during induction of epidural anesthesia? Anesthesiology 68:622–625, 1988
9. Chestnut DH, Weiner CP, Martin JG, et al: Effect of intravenous epinephrine upon uterine artery blood flow velocity in the pregnant guinea pig. Anesthesiology 65:633–636, 1986
10. Chestnut DH, Weiner CP: Monitoring maternal heart rate during epidural injection of a test dose containing epinephrine [letter]. Anesthesiology 64:839–840, 1986
11. Dawkins CJM: Analysis of the complications of extradural and caudal block. Anaesthesia 24:55–563, 1969
12. DeSimone CA, Leighton BL, Norris MC, et al: The chronotropic effect of isoproterenol is reduced in term pregnant women. Anesthesiology 69:626–628, 1988
13. Desparmet J, Mateo J, Ecoffey C, et al: Efficacy of an epidural test dose in children anesthetized with halothane. Anesthesiology 69:A774, 1988
14. Fong J: Ephedrine as a marker of intravascular injection in laboring parturients. Reg Anesth 15:271–272, 1990
15. Grice SC, Eisenach JC, Dewan DM, et al: Evaluation of 2-chloroprocaine as an effective intravenous test dose for epidural anesthesia. Anesthesiology 67:A627, 1987
16. Griffin RM, Scott RPF: A comparison between the midline and paramedian approaches to the extradural space. Anaesthesia 39:584, 1984
17. Guinard JP, Mulroy MF, Carpenter RL, et al: Test doses: Optimal epinephrine content with and without acute beta-adrenergic blockade. Anesthesiology 73:386, 1990
18. Guinard JP, Mulroy MF, Carpenter RL, et al: Epidural epinephrine test doses: Influence of aging. Anesthesiology 73:A773, 1990
19. Heller PJ, Goodman C: Use of local anesthetics with epinephrine for epidural anesthesia in preeclampsia. Anesthesiology 65:224–226, 1986
20. Hood DD, Dewan DM, James FM: Maternal and fetal effects of epinephrine in gravid ewes. Anesthesiology 64:610–613, 1986
21. Johnson PW, Hom M, Mulroy MF: Adequacy of automated blood pressure cuffs with epinephrine test doses in beta blocked patients. Anesthesiology 67:A187, 1987
22. Kenepp NB, Gutsche BB: Inadvertent intravascular injections during lumbar epidural anesthesia. Anesthesiology 54:172–173, 1981

23. Konstadt SN, Louie EK, Black S, et al: Intraoperative detection of patent foramen ovale by transesophageal echocardiography. Anesthesiology 74:212–216, 1991
24. Kopacz DJ, Mulroy MF: Chloroprocaine and lidocaine decrease hospital stay and admission rate after outpatient epidural anesthesia. Reg Anesth 15:19, 1990
25. Landry DP, Oriol NE: Comments on the problems associated with epidural test dosing. Reg Anesth 15:154, 1990
26. Leighton BL, DeSimone CA, Norris MC, et al: Isoproterenol is an effective marker of intravenous injection in laboring women. Anesthesiology 71:206–209, 1989
27. Leighton BL, Norris MC, DeSimone CA, et al: The air test as a clinically useful indicator of intravenously placed epidural catheters. Anesthesiology 73:610–613, 1990
28. Leighton BL, Norris MC, Sosis M, et al: Limitations of epinephrine as a marker of intravascular injection in laboring women. Anesthesiology 66:688, 1987
29. Marx GF: Cardiotoxicity of local anesthetics—The plot thickens [editorial]. Anesthesiology 60:3–5, 1984
30. Montamat SC, Davies AO: Physiological response to isoproterenol and coupling of beta-adrenergic receptors in young and elderly human subjects. Journal of Gerontology: Medical Sciences 44:M100–M105, 1989
31. Moore DC, Batra M: The components of an effective test dose prior to epidural block. Anesthesiology 55:693–696, 1981
32. Neal JM, Mackey DC, Harrington BE, et al: 2-Chloroprocaine and bupivacaine are unreliable indicators of intravascular injection in the premedicated patient. Anesthesiology 69:A357, 1988
33. Popitz-Bergez F, Datta S, Ostheimer GW: Intravascular epinephrine may not increase heart rate in patients receiving metoprolol. Anesthesiology 68:815–816, 1988
34. Roetman KJ, Eisenach JC: Evaluation of lidocaine as an intravenous test dose for epidural anesthesia. Anesthesiology 69:A669, 1988
35. Rooke GA, Bledsoe SW: Failure of an epinephrine test dose to elicit tachycardia after intravascular epidural catheter placement. Reg Anesth 15:147–149, 1990
36. Scott DB: Test dose in extradural block [editorial]. Br J Anaesth 61:129–130, 1988
37. Sidi A, Rush WR, Paulus DA, et al: Effects of fluorescein, indocyanine green, and methylene blue on the measurement of oxygen saturation by pulse oximetry. Anesthesiology 65:A132, 1986
38. Soni V, Peeters C, Covino B: Value and limitations of test dose prior to epidural anesthesia. Reg Anesth 6:23–25, 1981
39. Van Zundert A, Vaes L, Soetens M, et al: Identification of inadvertent intravenous placement of an epidural catheter in obstetric anesthesia. Anesthesiology 68:142–145, 1988
40. van Zundert A, Vaes L, Soetens M, et al: Every dose given in epidural analgesia for vaginal delivery can be a test dose. Anesthesiology 67:436–440, 1987
41. Verniquet AJW: Vessel puncture with epidural catheters: Experience in obstetrical patients. Anaesthesia 35:660, 1980
42. Vestal RE, Wood AJJ, Shand DG: Reduced beta-adrenoreceptor sensitivity in the elderly. Clin Pharmacol Ther 26:181, 1979
43. Youngstrom P, Cohen I, Hoyt M, et al: Effects of intravenous test dose epinephrine on fetal sheep during acute fetal stress and acidosis. Reg Anesth 15:237–241, 1990
44. Zuspan FP, Nelson GH, Ahlquist RP: Epinephrine infusion in normal and toxemic pregnancy. Am J Obstet Gynecol 90:88–98, 1964

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HISTORY OF EPIDURAL ANESTHESIA

Justifiably dubbed the Cadillac of pain relief, epidural analgesia remains the "only effective" way to treat labor pain.[93] In 1901, Sicard and Cathelin independently introduced caudal analgesia into anesthetic practice. Von Stoeckel later administered caudal blocks for obstetric pain, but mothers had unsatisfactory analgesia, mainly due to drug limitations.[3, 48] Lowen, in 1910, successfully employed epidural block for pelvic and abdominal surgery and injected procaine, 1.5% to 2%, via a sacral hiatus into the cauda equina region. Sicard (1921) first described loss of resistance (LOR) to fluid injection for epidurography, while Pages popularized the midline approach to the lumbar epidural space (LES). In pioneer work, Aburel, in 1931, first described continuous epidural (caudal) lumboaortic plexus block for childbirth pain (although Dogliotti, who popularized lumbar epidural analgesia [LEA] in Italy, is often considered the father of obstetric analgesia).[31] Aburel also identified the double sensory innervation of the uterus, from sympathetic and "cerebrospinal" fibers, and his diagrams of nociceptive pathways clearly demonstrated the dual supply, extending from T12 to L2 and S2 to S4. Aburel introduced a soft silk catheter via the epidural needle and gave repeated injections of cinchocaine, 0.5%. He also tried other local anesthetics, but achieved his best results with 0.5% cinchocaine plus 1:100,000 epinephrine, which lasted for 3 to 5 hours.

Cleland,[27] in 1933, also described the sensory innervation of the birth canal and gave lower thoracic paravertebral and caudal block for obstetric pain relief. Hingson and Edwards,[60] in 1942, introduced a

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flexible, malleable, steel needle for continuous caudal analgesia, and by 1943, reported 1000 cases. Hingson and Southworth[59] later published their experiences of LEA, using a spinal needle and ureteric catheter. Tuohy invented his needle in 1945 and used a catheter-through-the-needle approach for continuous spinal anesthesia. Flowers et al[43] and Curbelo[30] adapted Tuohy's technique to pass a ureteric catheter into the LES. Finally, Cleland[26] developed his two-catheter technique: an upper catheter at thoracolumbar level for first-stage analgesia, and the lower catheter via the sacral hiatus, for second-stage analgesia.

Although practitioners like Hingson, Edwards, and Cleland popularized LEA in North America, the technique only became widely disseminated in the late 1960s, when Bonica published his magnum opus *Principles and Practice of Obstetric Analgesia and Anesthesia,*[10] and several international practitioners reported their experience of LEA at the 4th World Congress of Anaesthesiology.

PHILOSOPHY OF OBSTETRIC ANALGESIA

Effective pain relief throughout labor requires consecutive analgesia of thoracolumbar and sacral pathways. Practitioners of caudal analgesia recognized disadvantages of the technique, including fetal malrotation, because the early perineal anesthesia contributed to pelvic floor relaxation. Modern practice owes much to the philosophy of Doughty, who coined the term "selective epidural analgesia" to describe predominantly thoracolumbar analgesia, achieved with small anesthetic doses.[39] Only 19% of Doughty's patients who delivered spontaneously requested sacral analgesia in the second stage. Although he recognized that fortuitous spread of local anesthetic sometimes obtunded perineal sensation, Doughty described the following advantages of his selective technique: preservation of pelvic floor tone, allowing normal rotation of the fetal head; retention of vaginal (or rectal) pressure, enabling the mother to focus expulsive efforts; and small drug doses in first stage labor, thus limiting side effects. Doughty reported a spontaneous delivery rate of 80% in normal subjects. Contemporary practice seeks to minimize maternal motor block, while achieving excellent sensory analgesia, and a trend toward ambulatory pain relief has emerged. The use of very dilute bupivacaine concentrations (0.0312%), with the addition of opioids, e.g., sufentanil, exemplifies this trend.[83]

BENEFITS OF EPIDURAL ANALGESIA IN LABOR

Morgan and associates,[80] in a comparative study of 1000 mothers, confirmed that LEA gave superior pain relief and proved "strikingly more effective" than systemic medications, inhalational analgesia, and pudendal block. A recent prospective study asked parturients to compare LEA and meperidine, with respect to analgesic efficacy and mothers' feelings and symptoms during labor and delivery.[86] The analgesia from LEA proved significantly superior to meperidine. Fifty-nine percent of women in the epidural group had painless labor and delivery, compared with 20% in the meperidine group ($P < 0.001$). Ninety per cent of all parturients wanted analgesia in a future labor. Of the epidural group, 73% wanted another epidural, whereas only 30% of the meperidine group would accept meperidine again.

Reynolds[93] says consumers often class epidural block with obstetric interventions as "an undesirable interference by the medical profession, in what would otherwise be a trouble-free and satisfying natural event." However, LEA prevents the adverse biochemical changes associated with labor and, in appropriate doses, does not abolish the pain of abruption or imminent rupture of a uterine scar. In complicated labors, e.g., preeclampsia, twins, breech presentation, and vaginal birth after cesarean section, LEA enables mothers to be prepared for immediate intervention, such as cesarean section. Importantly, in contrast to systemic narcotics, LEA does not delay gastric emptying.

Maternal disadvantages include the need for an intravenous line, occasional dizziness, postural hypotension, weakness of the legs, and difficulty emptying the bladder.[93] Shivering, "a tiresome complication," which opioids help,[98] and maternal pyrexia are other possible consequences.[45] Reynolds also refers to the occasional lack of perfect analgesia that mothers justifiably resent, and the disadvantages of accidental dural puncture, including infrequent sixth nerve palsy. Serious sequelae, such as epidural hematoma, accidental total spinal anesthesia, and local anesthetic toxicity, rarely occur.

Reynolds[93] considers the fetal benefits of LEA "unequivocal." Fetal acidosis occurs only if the mother develops severe hypotension that goes untreated. Otherwise, beneficial biochemical changes occur, with little deterioration in fetal acid–base status during second-stage labor, even if prolonged. The fetal circulation also improves. Delivery under epidural block is less traumatic, and neonatal retinal hemorrhages occur less frequently. The condition of second twins, at delivery, is substantially better after LEA than with other techniques. Neonates also fare better. David and Rosen[34] surveyed over 6000 births, and demonstrated less neonatal mortality, especially for low-birth-weight babies, when mothers had epidural analgesia.

ANATOMY OF THE EPIDURAL SPACE

The epidural space extends from foramen magnum to sacral hiatus and surrounds the spinal cord (enveloped in its dural sac) throughout its length.[48] Anteriorly, it is bounded by the posterior longitudinal ligament, which covers the posterior aspect of all vertebral bodies and intervertebral disks. The vertebral pedicles and intervertebral foraminae through which the spinal nerves exit lie laterally. Posteriorly, the anterior surface of the vertebral laminae and ligamenta flava complete the boundaries of the space. The fibers of ligamentum flavum run vertically and connect the upper and lower borders of adjacent laminae. Because the spinal cord terminates opposite the lower border of L1, or upper border of L2, an obstetric epidural usually involves a lumbar approach, to minimize the risk of cord damage.

Recent studies demonstrated the triangular shape of the vertebral canal in the lumbar region.[41] The apex of the triangle forms a sulcus posteriorly, between right and left ligamenta flava. Gaynor[48] says the ligament is seldom a continuous band of tissue spanning the space between laminae; in most cases, the two ligamenta lie at an angle of greater than 90 degrees to one another, with a discrete gap between their medial borders. They are also thinner (approximately 3 mm) than was previously supposed.

The epidural space contains the rich internal vertebral venous plexus, with two prominent longitudinal veins running alongside one another in the anterolateral region of the vertebral canal. In pregnancy, these veins become engorged as a result of inferior vena cava compression by the pregnant uterus. The plexus then forms a bypass between internal iliac veins and the intercostal and azygos systems. The spinal cord derives its arterial supply from anterior and posterior spinal arteries. The larger, anterior artery lies in the anterior median fissure and receives contributions from segmental arteries, which, in turn, derive from vertebral, intercostal, and iliac arteries. The smaller posterior spinal arteries, situated posterolaterally on each side of the midline, also derive their supply from segmental vessels throughout the length of the vertebral column. An epidural catheter may traumatize or cannulate an epidural vein; some authors consider this risk greater with the midline approach to the epidural space.[48] A remote risk of arterial trauma, from an epidural cannula, may exist when the artery of Adamkiewicz arises at the lumbar, instead of thoracic, level. Bromage[12] and Gaynor[48] discuss this possibility in greater detail. In addition to blood vessels, the epidural space contains fat (mainly, posteriorly) and fibrous connective tissue strands.

The recent introduction of nuclear magnetic resonance imaging and developments in epidurography have added to our knowledge of epidural space anatomy in living subjects.[48] Throughout its length, spinal dura is closely apposed to the walls of the vertebral canal and the contents of the epidural space, reflecting Bromage's description of the space as "potential."[12] Blomberg and Olsson[6] visualized the LES in eight of ten nonpregnant subjects by percutaneous epiduroscopy. They noted that dura mater lay very close to the dorsal aspect of the epidural space, and they observed a dorsomedian connective tissue band, attaching dura to the ligamenta flava (Figs. 1 and 2). The band caused a dorsal fold in the dura and was seen in all subjects.

Harrison and Clowes[56] examined the depth of the LES at different interspaces in 1000 parturients and found its median distance from skin to be 4.7 cm. In only 5% of subjects did it exceed 7 cm. The distance from the posteromedial border of ligamentum flavum to dura mater is greatest in the second lumbar interspace, and ranges between 4 and

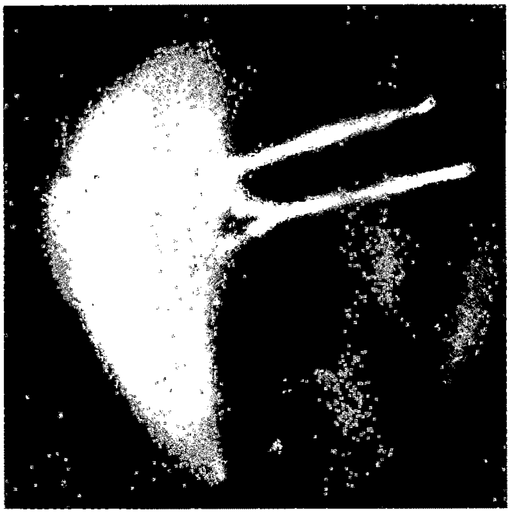

Figure 1. Epiduroscopy, caudal view. The dura mater is on the left and the ligamenta flava on the right. Injection of air into the epidural space has opened up the space, revealing some strands of connective tissue in the dorsomedian band. (*From* Blomberg RG, Olsson SS: The lumbar epidural space in patients examined with epiduroscopy. The International Anesthesia Research Society. Anesth Analg 68:157–160, 1989; with permission.)

8 mm. An epidural needle, inserted by the midline approach, should enter the space as close to the midline as possible, to maximize the distance between ligamentum flavum and dura.

When viewed laterally, with nuclear magnetic resonance imaging, the dural sac has a saw-toothed appearance. At the level of each lamina, dura is closely applied to periosteum, while its furthest distance from ligamentum flavum occurs opposite each interspace.[48]

PHYSIOLOGIC EFFECTS OF EPIDURAL BLOCK

The primary locus of action of epidural local anesthetics appears to be the dorsal root ganglia, but paravertebral and centripetal (neurax-

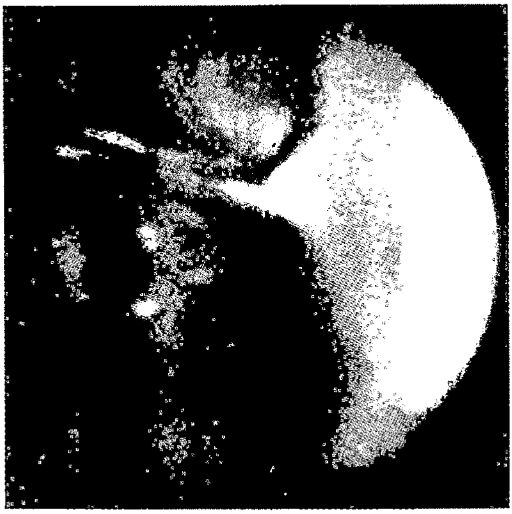

Figure 2. Epiduroscopy, caudal view. The dura mater is on the right, and the ligamenta flava to the far left. Clearly visible is a prominent dorsomedian connective tissue band, which attaches the dura mater to the dorsal aspect of the epidural space. (*From* Blomberg RG, Olsson SS: The lumbar epidural space in patients examined with epiduroscopy. The International Anesthesia Research Society. Anesth Analg 68:157–160, 1989; with permission.)

ial) spread occurs later. A, B, and C fibers differ in their minimum blocking concentrations, not only as a function of fiber diameter. Studies also demonstrate that nerves from pregnant animals have an increased susceptibility to local anesthetics.[33] In clinical practice, sympathetic (B fiber) blockade inevitably accompanies the onset of LEA and, in consequence, systolic and diastolic blood pressures should be recorded following institution of the block. Hughes and colleagues[62] performed Doppler velocimetry of the maternal uterine and fetal umbilical arteries in term parturients in active labor. Maternal systolic and diastolic blood pressures and pulse rates declined with institution of the block, but no women experienced hypotension. Mean systolic/diastolic ratios, and pulsatility indices of uterine and umbilical arteries, did not change significantly. The authors concluded that effective LEA does not significantly affect flow in maternal or fetal vessels, despite the lowered maternal blood pressure and pulse rate.

Deckardt and associates[35] studied the effects of labor pain on maternal SaO_2, and neonatal acid–base status. Maternal oxygenation and neonatal pH decreased significantly, presumably due to pain, in meperidine-treated mothers. Primipara having effective LEA showed a significantly smaller decrease in SaO_2 and better neonatal acid–base status, than did meperidine subjects. The authors did not, however, find these differences in multipara. Janbu[64] also demonstrated pain's adverse circulatory effects by comparing blood velocity in dorsalis pedis and radial arteries during labor in two groups of women: a control group with painful contractions and an epidural group with effective analgesia. In the control group, blood velocity, in both radial and dorsalis pedis vessels, demonstrated large fluctuations, probably due to temperature regulation. During contractions, velocity decreased by 80%, whether mothers were supine or lateral, presumably due to pain-induced vasoconstriction. In the epidural group, in contrast, blood velocities remained steadily high, in consequence of the effective block. Janbu's work confirms that, during painful contractions, lower extremity arteries exhibit vasoconstriction, which LEA abolishes. While the significance of these findings awaits further evaluation, they emphasize the need to establish early epidural block in mothers with significant vasoconstriction (e.g., pregnancy-induced hypertension [PIH]).

Fusi and colleagues[45] described maternal pyrexia, in association with LEA in labor. Forty women in spontaneous labor at term, who received meperidine or epidural analgesia, began with a normal temperature and no clinical evidence of infection. Mean oral and vaginal temperatures in the meperidine group remained constant during labor, whereas they increased significantly after 6 hours in the LEA group. The increase was unrelated to infection, and the authors suggested it may result from vascular and thermoregulatory changes induced by the epidural block. Analysis of baseline fetal heart rate showed it to be closely related to maternal temperature (R = 0.91). The number of vaginal examinations and use of fetal monitoring did not differ between groups. The authors believe these results confirm that women having LEA during labor develop positive heat balance, with a steady rise in vaginal and oral temperatures. In some, this progresses to clinical pyrexia, perhaps due to disturbed thermoregulation and an imbalance between heat-producing and heat-dissipating mechanisms. The maternal pyrexia can cause fetal pyrexia, persistent fetal tachycardia, and, in turn, fetal hypotension and metabolic acidosis. Persistent pyrexia requires appropriate action to reduce maternal temperature, e.g., sponging, and cooling with a fan.

EPIDURAL ANALGESIA AND THE PROGRESS OF LABOR

Studd and coworkers[100] evaluated the effect of LEA on the rate of cervical dilatation and outcome of spontaneous labors. An epidural block had no effect on the cervical dilatation rate, or duration of first-stage labor, but led to a 20-fold increase in rotational forceps delivery. Thorp et al[102] found an increase in the cesarean section rate for dystocia, following epidural block. They studied more than 700 consecutive nullipara at term, who received LEA, narcotics, or no pain relief. In the epidural group, 10% of women required cesarean section, in contrast to 4% in the nonepidural group. Significantly more women in the epidural group required oxytocin augmentation (73% versus 27%). When the authors excluded large babies (>4000 g) from both groups, the incidence of cesarean section for dystocia remained significantly greater in the epidural group (9% versus 3.2%).

Since 1987, Chestnut and associates[21, 23, 24] have studied the effects of continuous LEA with bupivacaine, plus or minus fentanyl, on second-stage labor and mode of delivery. Initially, they compared the effect of continuing a bupivacaine infusion (0.125% at 12–14 mL/h) with stopping the drug, and substituting saline, at 8 cm or greater cervical dilatation.[24] Mean duration of second-stage labor was significantly longer in the bupivacaine (B) group (124 versus 94 minutes) but 82% of B group subjects, versus 41% of the saline group, had analgesia of excellent or good quality. Fifty-three percent of women in the B group, versus 28% in the saline group, required instrumental vaginal delivery ($P < 0.05$). The authors concluded that bupivacaine, infused beyond 8 cm, gave satisfactory pain relief, but prolonged second-stage labor and increased the instrumental delivery rate. In 1988, Chestnut's group questioned if addition of fentanyl to dilute bupivacaine would provide analgesia similar to bupivacaine alone, and whether the lessened motor block from the combination would shorten second-stage labor.[23] Analgesia was maintained by continuous epidural infusion (CIEA) of bupivacaine 0.0625%/fentanyl 0.0002% (BF), or bupivacaine alone (0.125%) (B). The investigators discontinued the infusion at full cervical dilatation. During first-stage labor, both groups had comparable analgesia, but women in the B group were more likely to have motor block. The authors found no significant difference in duration of second-stage labor, mode of delivery, or neonatal status, and concluded that CIEA, with BF, produced analgesia similar to B alone. However, the less intense motor block in the BF group did not shorten second-stage labor or increase spontaneous deliveries.

In their third study, these workers used 0.0625% bupivacaine/ 0.0002% fentanyl in all subjects, until full cervical dilatation.[21] During second-stage labor, one group had saline placebo, whereas CIEA was maintained in the other group. Pain was significantly greater in the saline group at each 30-minute interval, between 60 and 150 minutes after full cervical dilatation, but the authors found no significant difference in duration of second-stage labor, instrumental deliveries, or neonatal status. Therefore, stopping the BF infusion at full dilatation causes pain and does not increase the likelihood of spontaneous delivery.

Bates and colleagues[4] identified diminished uterine activity, in second-stage labor, in primigravid and multiparous women having LEA. The authors suggested the decreased uterine activity contributed to prolongation of the second stage and increased instrumental delivery. One possible explanation is lack of the normal oxytocin surge at full cervical dilatation. Goodfellow et al[49] measured second-stage plasma oxytocin levels in primigravid women having effective LEA or systemic medication. A significant rise occurred in the nonepidural group, but the authors found no such increment in the LEA group. Instrumental delivery was required more frequently in the LEA group and was associated with lower oxytocin levels at crowning. Goodfellow et al believe LEA inhibits the normal oxytocin release, caused by distension of the lower birth canal and stimulation of pelvic autonomic nerves. They recommend parenteral oxytocin in second-stage labor to enhance uterine activity. Saunders et al[96] started oxytocin at full cervical dilatation, in women having LEA, and achieved a reduction in nonrotational forceps deliveries and perineal trauma. However, oxytocin did not correct fetal malrotation.

Maresh and his group[75] evaluated delayed pushing to manage second-stage epidural labor. In an early pushing group, subjects pushed as soon as they felt an urge. The mean waiting time to commencement of pushing was 27 minutes. In the delayed group, pushing was delayed for up to 2 hours and 30 minutes. An increase in the spontaneous delivery rate, not reaching statistical significance, occurred in the delayed pushing group. Delay did not increase the incidence of abnormal fetal heart rate or affect neonatal status.

No consensus exists on the appropriate management of second-stage epidural labor, but the following principles apply: (1) analgesia should be maintained (allowing the epidural to wear off will not increase the likelihood of spontaneous delivery); (2) early, ineffective pushing should be discouraged; and (3) inefficient uterine contractions should be augmented by oxytocin infusion.

INDICATIONS FOR EPIDURAL ANALGESIA IN LABOR

Maternal indications for epidural analgesia in labor[74] include (1) maternal pain, the primary indication; (2) maternal request or preference; (3) dysfunctional labor, especially in primigravidae; (4) oxytocin-induced/augmented labor; (5) vaginal birth after cesarean section; (6) anticipated difficult intubation; and (7) maternal disease, such as hypertensive disease (e.g., PIH, essential hypertension), respiratory disease (e.g., asthma, cystic fibrosis), renal disease (especially postrenal transplant), neurologic and neuromuscular disease (including multiple sclerosis and quadriplegia, especially if associated with autonomic hyperreflexia), some cardiac diseases, endocrine disease (e.g., diabetes, and morbid obesity), and musculoskeletal disease.

Fetal indications include (1) prematurity and intrauterine growth retardation, (2) breech presentation undergoing trial of vaginal delivery, (3) multiple pregnancy (invariably, twins), (4) trial of vaginal delivery, and (5) Rh hemolytic disease.

As experience with epidural analgesia increases, the recommended contraindications diminish, and some recent case reports emphasize its benefits in very high risk parturients. Brian et al[11] used LEA in a quadriplegic woman with autonomic hyperreflexia and premature labor at 29 weeks gestation. With contractions, she experienced hypertensive episodes, flushing, and sweating of the head and neck. She underwent cesarean section with epidural anesthesia, and, although she required trimethaphan to control hypertension during incision, remained stable throughout surgery. Abouleish et al[2] described a similar parturient with C4-5 quadriplegia and autonomic hyperreflexia, characterized by severe headaches, blurred vision, sweating, and lower limb spasms, which signalled the onset of labor. Epidural fentanyl, 75 μg, failed to control the autonomic hyperreflexia, but a bolus of bupivacaine, 0.25%, 15 mL, followed by continuous bupivacaine infusion, secured cardiovascular stability. Robinson and Leicht[94] used epidural bupivacaine/fentanyl in a parturient with severe pulmonary hypertension. They made hemodynamic measurements throughout, and, with stronger contractions, pulmonary artery pressure trended steadily upward, and cardiac output declined. A bupivacaine/fentanyl infusion, 10 mL/h, gave excellent analgesia. Minnich et al[78] gave LEA to a parturient with hypertrophic obstructive cardiomyopathy having induction of labor at 36 weeks gestation. She had an early epidural with bupivacaine, 0.125%, plus fentanyl 5 μg/mL, and received top-up doses of this combination to provide adequate relief. Management of anesthesia included: ECG, pulmonary artery catheter, and continuous arterial pressure monitoring. Perineal anesthesia was achieved with bupivacaine, 0.25%, in 10-mL increments. The patient remained very comfortable throughout labor and delivery, and Minnich considered the technique a viable alternative for such patients.

Finer and coworkers[42] successfully employed continuous LEA in a primigravida with documented sickle-cell disease. She had a 24-hour history of abdominal pain and severe diffuse lower extremity joint pain, similar to her usual sickling crises. Intermittent top-ups of 0.25% bupivacaine, throughout labor, controlled the crisis pain, and gave good labor analgesia. After delivery, an epidural fentanyl infusion (5 μg/mL, at 8 mL/h) maintained her pain free for approximately 12 hours.

The authors believe epidural analgesia with local anesthetics, opioids, or both, may have promise in selected patients with sickle-cell anemia with vaso-occlusive crises.

CONTRAINDICATIONS TO EPIDURAL ANALGESIA

Absolute contraindications to epidural analgesia include (1) patient refusal, (2) nonavailability of anesthesiology and supportive staff, (3) systemic (or severe local) sepsis, (4) major bleeding diatheses, and (5) increased intracranial pressure. Relative contraindications include (1) maternal hypovolemia (requires correction before initiating block), and (2) some coagulopathies. Although epidural anesthesia has been successfully employed in women with cerebral tumor, Chater et al[18] suggest that increased intracranial pressure should contraindicate the technique because of the unpredictable incidence of dural tap.

TECHNIQUES OF EPIDURAL ANALGESIA

Lumbar Epidural: Midline or Paramedian Approach?

Autopsy studies by Blomberg[7] compared the midline and paramedian approaches to the LES, with respect to the risk of accidental dural puncture, the course of the epidural catheter after introduction, and the influence of the dorsomedian connective tissue band. With the paramedian approach, the epidural needle traversed a greater distance within the space before it contacted dura mater, and the smooth convex portion of its tip came to lie adjacent to dura, pushing it away, rather than perforating it, suggesting a low risk of dural puncture. With the midline approach, the bevel of the epidural needle came directly into contact with dura, almost at 90 degrees. A catheter inserted by the paramedian approach did not tent dura and took a straight cephalad direction in all cases. Midline catheters, in contrast, tented dura, and their direction of travel proved very variable. The dorsomedian connective tissue band exerted its greatest influence on the behavior of the midline-inserted needle and catheter. Carrie[15] also strongly advocates the paramedian approach and considers it easier to teach (and learn) because the laminae form a precise bony landmark. He advances the Tuohy needle at right angles to all skin planes, 15 mm lateral to the cephalad end of the spinous process below the desired interspace. The needle traverses paravertebral muscles, then contacts the lamina. After injection of additional local anesthetic, the needle is partially withdrawn, redirected toward the midline with more cephalad angulation, and readvanced. The paramedian approach requires less flexion of the back and may be preferable when patients find flexion difficult.

Griffin and Scott[53] compared the two approaches in a prospective randomized study of parturients. Both approaches proved comparable in success rate, ease of catheter insertion, and incidence of complications. However, 28% of women having the paramedian approach complained of moderate-to-severe pain, compared with 18% of those undergoing the midline approach ($P < 0.05$), and the authors recommended more infiltrated local anesthetic for the paramedian approach.

Caudal

Because of early perineal anesthesia, caudal block has generally "fallen from grace" in first-stage analgesia. It may prove useful for second- and third-stage procedures and in special situations (e.g., previous lumbar spine surgery). It also results in the administration of more local anesthetic.

Spinal-Epidural

Carrie[14] recently described combined spinal-epidural techniques for obstetric surgical anesthesia. At present, these techniques have minimal acceptance in labor. However, Gutsche (personal communication, 1990) inserts a 4.5-inch, 24-gauge Sprotte (or finer spinal needle) through a 3.5-inch epidural needle and injects subarachnoid fentanyl, 37.5 μg. He then removes the Sprotte needle and inserts an epidural catheter for later administration of local anesthetics.

LOCAL ANESTHETICS IN EPIDURAL ANALGESIA

Bupivacaine remains the local anesthetic of choice for labor analgesia. In a comparative study of bupivacaine, lidocaine, and chloroprocaine, Abboud et al[1] observed a mean duration of pain relief from 0.5% bupivacaine of 115 (SD, 36) minutes, compared with 52 (18) minutes for 1.5% lidocaine, and 46 (14) minutes for 2% chloroprocaine. All agents gave comparable pain relief and did not differ in their maternal effects. Although none had a significant effect on baseline fetal heart rate or beat-to-beat variability, late fetal decelerations occurred more frequently after bupivacaine. The significance of this finding remains unclear. Lidocaine, 1.5%, gives equally effective pain relief, but of shorter duration. However, lidocaine causes more motor block than bupivacaine in equianalgesic concentrations, and in my practice, I reserve it for specific situations in labor analgesia. For example, in second-stage labor, when the fetal head remains high (e.g., persistent occipitoposterior position) 1% lidocaine (plus epinephrine 1:400,000) provides good motor and sensory block to facilitate rotation of the fetal head. 2-Chloroprocaine, in my view, has little application in labor analgesia, because of its short duration and rapid offset. However, many anesthesiologists prefer to initiate the block with chloroprocaine, because of its rapid onset and inherent safety.

The elimination half-life of bupivacaine in parturients is 6 to 9 hours, and maternal plasma concentrations increase with the dose (whether plain bupivacaine or bupivacaine plus epinephrine).[91] Flynn and colleagues[44] compared plasma bupivacaine concentrations during CIEA, in parturients receiving either 0.25% or 0.08% at a comparable rate, 20 mg/h. Plasma concentrations were significantly lower in subjects having the weaker solution. Umbilical artery and vein concentrations equilibrate rapidly following each dose, suggesting that bupivacaine approaches equilibrium across the placenta in a single circulation.[91] Equilibration in the whole fetal compartment takes less than 1 hour.

pH Adjustment of Local Anesthetics

McMorland's group[76] gave pH-adjusted bupivacaine to parturients having LEA. The addition of 0.1 mmol, 8.4% $NaHCO_3$, to 20 mL, 0.25% bupivacaine, consistently raised bupivacaine's pH from 5.56 to a mean of 7.26. Onset time of analgesia decreased from 6.0 to 3.2 minutes, and duration increased from 79 to 96 minutes. DiFazio et al[37] observed a similar effect with pH-adjusted lidocaine. Latency of onset varied inversely with pH of the injected local anesthetic and decreased progressively as the pH of lidocaine increased toward 7.2. pH adjustment also increased sensory spread. Chestnut and associates[22] adjusted the pH of 2% chloroprocaine, by adding 1 mL 8.4% $NaHCO_3$ to each 30-mL vial. Onset of pain relief occurred slightly more rapidly in the pH adjusted group (12 versus 14 min). Quality of analgesia also improved; 2 of 31 women in the pH-adjusted group, versus 10 of 31 in the control group, required additional chloroprocaine to achieve satisfactory analgesia. However, the authors did not consider these results sufficiently compelling to recommend routine pH adjustment of chloroprocaine.

Addition of Epinephrine to Local Anesthetics

As well as possessing vasoconstrictor properties, epinephrine has an α-adrenergic analgesic effect, mediated through dorsal horn gray matter. Eisenach and colleagues[40] demonstrated its effectiveness in parturients who received either 0.25% bupivacaine plain, or plus 1:300,000 epinephrine. Epinephrine enhanced bupivacaine analgesia; significantly fewer subjects in the epinephrine group required additional local anesthetic to secure initial pain relief. Epinephrine also decreased bupivacaine's latency of onset, from 8.7 to 5.8 minutes, and significantly prolonged analgesia from 92 to 123 minutes. Hypotension did not differ between groups, but the epinephrine group had a significantly higher heart rate following the block. Potential complications of epinephrine include decreased uterine blood flow, possible prolongation of labor, and the hazards of intravenous injection. Eisenach's group[50] also investigated enhancement of BF analgesia by epinephrine. In random manner, parturients received either 0.25% bupivacaine, 10 mL, plus 5 μg/mL fentanyl, or 10 mL of BF, plus 3.33 μg/mL freshly added epinephrine. Epinephrine prolonged the mean duration of pain relief (180 versus 130 minutes).

Addition of Opioids to Local Anesthetics

The 1980s witnessed many studies evaluating addition of opioids to local anesthetics for labor analgesia. Early work by Justins et al[68] demonstrated that extradural fentanyl, 80 μg, significantly prolonged bupivacaine analgesia and reduced the number of mothers who needed additional bupivacaine to establish relief. Many studies have since confirmed that fentanyl, 50 to 150 μg, when added to bupivacaine, 0.125% to 0.5%, provides better pain relief than local anesthetic alone, increasing both duration and quality of analgesia.[28, 66, 67, 71] (The combination of fentanyl with 0.125% bupivacaine, for example, gives comparable pain relief to 0.25% bupivacaine alone.[23]) Lirzin and coworkers[71] compared bupivacaine/fentanyl with bupivacaine/morphine in labor. Fentanyl, 80 μg, significantly increased the duration of 0.25% bupivacaine (132 versus 97 minutes), whereas morphine did not influence duration of analgesia and actually increased the frequency of inadequate pain relief. Jones et al[66] compared a bolus of 0.5% bupivacaine, plus fentanyl, 100 μg, followed by epidural infusion of 0.08% bupivacaine, plus fentanyl 2.5 μg/mL, at 15 mL/h, with the same regimen using bupivacaine only. Fentanyl significantly prolonged the time from loading dose to the first top-up. However, 75% of mothers given fentanyl experienced pruritus, compared with 5% in the control group.

Reynolds and O'Sullivan[92] compared bupivacaine, 0.25%, fentanyl, 100 μg, and fentanyl, 100 μg in bupivacaine, 0.1%, to treat perineal pain during first-stage labor. Fentanyl plus bupivacaine gave consistently reliable pain relief, quicker in onset and longer in duration: 140 versus 114 minutes (fentanyl alone) versus 99 minutes (bupivacaine alone). Side effects (pruritus and drowsiness) occurred more frequently in the fentanyl groups, but were not troublesome.

In a recent editorial, Reynolds[93] offers, in my view, a pessimistic assessment of opioids. She questions if the gain in improved pain relief from fentanyl outweighs the inconvenience of using a controlled drug. Indeed, she cites only two distinct advantages for opioids: (1) the management of perineal pain, and (2) effective management of shivering due to epidural block. My answer to her question is a resounding yes. I consider the advantages of routine fentanyl addition self-evident from the previously mentioned research and find pruritus, the only major side effect, rarely troublesome.

Phillips[88] compared sufentanil, 10, 20, and 30 μg, and saline added to 0.25% bupivacaine. All subjects had good analgesia, but relief was much greater in those who received 30 μg sufentanil than in saline controls. Thirty minutes after institution of the epidural, pain scores in the four groups were similar, suggesting that, although sufentanil, 30 μg, hastened the onset of pain relief, it did not affect quality of analgesia. However, the duration of analgesia was increased by sufentanil (144 versus 90 minutes). In the van Steenberge group,[103] randomized parturients received 10 mL of 0.125% bupivacaine plus epinephrine (1:800,000), alone, or with the addition of sufentanil, 7.5 or 15 μg. On request, subjects received a second injection identical to the first, then subsequent injections of bupivacaine/epinephrine as needed. Sufentanil significantly shortened onset of analgesia and increased its duration. Pain relief lasted a mean of 130 minutes in the sufentanil groups, compared with 86 minutes in the control group. Sufentanil recipients required less bupivacaine throughout labor and had less motor block at delivery. In the sufentanil groups 20% to 40% of women experienced pruritus. Naulty et al[83] concluded that 5 μg sufentanil significantly potentiates bupivacaine analgesia and enables extremely low concentrations (e.g., 0312%) to be effective.

Hunt and coworkers[63] studied butorphanol, 1, 2, or 3 mg, added to 0.25% bupivacaine. The optimal dose (2 mg) significantly prolonged bupivacaine analgesia (137 versus 59 minutes), shortened its onset (7 versus 21 minutes), and enabled a 50% reduction in the subsequent bupivacaine dose. The authors considered 2 mg a safe adjunct to bupivacaine in labor, but 3 mg caused maternal somnolence and a low amplitude, sinusoidal fetal heart rate.

Brownridge[13] prospectively studied 100 women who received bupivacaine, 0.125%, plus meperidine, 25 mg, for institution of epidural block. Subsequent top-ups of 0.25% to 0.5% bupivacaine or bupivacaine/meperidine were given when pain relief became inadequate or in preparation for instrumental delivery. Mean duration of pain relief was 83 minutes, with considerable individual variation. Sixty-two per cent of mothers felt more relaxed, calm, or euphoric; 15% successfully stood or walked during labor. Fifteen per cent experienced nausea. No shivering occurred in the study, and only seven subjects complained of pruritus, a clear benefit of meperidine. Brownridge identified other benefits of adding meperidine: patient mobility, awareness of bearing down, and, although this was not a double-blind study, an increased likelihood of normal delivery (63% primigravid, 90% multiparous).

PRACTICAL ASPECTS OF EPIDURAL ANALGESIA FOR LABOR

Informed Consent

Knapp[69] analyzed three legal cases that addressed adequacy of anesthetic consent during labor, and each court decided the issue in favor of the anesthesiologist. Three common factors supported their finding of informed consent: information given to the patients, the lack of objection by the patients, and the cooperation given by patients during performance of the procedure. Knapp concludes that acquiring anesthetic consent during labor should not be viewed as impossible, or even academic. Grice et al[51] evaluated laboring women to determine their competence to give informed consent for anesthesia in labor. Women were randomly assigned to one of two groups: verbal or verbal plus written consent. All preanesthetic interviews were performed by one of the authors and included discussion of anesthetic options, procedures and risks, with the use of a checklist. Following discussion, the verbal plus written consent group received a written consent form, which reiterated the topics discussed. Participants were telephoned 5 to 7 months later by an investigator unaware of the group to which they belonged, and asked ten objective questions to evaluate recall of the consent process. The verbal plus written consent group had significantly higher recall scores. The authors believed written consent provided tangible evidence of the topics discussed, and verbal plus written consent gave parturients improved recall.

Equipment and Related Factors

Equipment, facilities, and trained personnel must be appropriate for immediate resuscitation and life support, in all locations where LEA is given. Complications such as total spinal anesthesia or local anesthetic toxicity can occur rapidly, leading to respiratory or circulatory arrest. Yarnell[104] describes a portable cart to facilitate labor room placement of epidurals. The cart combines monitoring equipment, a light source, epidural supplies, resuscitation drugs, and equipment. All labor rooms in his institution have independent O_2 and suction, as well as a supply of oral airways, resuscitation bag, and mask. On initiation of an epidural, the cart is moved to the patient's bedside and monitors attached, including automated blood pressure and pulse oximeter.

Michael et al[77] studied 802 women having LEA to compare open-ended, single-hole epidural catheters with closed-end catheters having three lateral holes. The number of unsatisfactory blocks increased significantly with single-hole catheters (131/401 as opposed to 55/401). Seventy-eight percent of unilateral blocks and 72% of missed segments occurred with single-hole catheters. Closed-end catheters were easier and less painful to insert, but the authors noted a higher incidence of bloody taps with their use (42/401 versus 23/401). Power and Thorburn[89] studied differential flow from multihole catheters. As injection pressure increases, flow appears initially at the proximal, then the middle, and finally the distal hole. Thus, the effect of epidural doses, given through multihole catheters, may vary with injection pressure. When a catheter partially enters dura, for example, differential exit of local anesthetic depends, among other factors, on injection pressure; forceful injection increases the likelihood of subarachnoid block.

Loss of Resistance: Saline or Air?

Dalens and associates[32] reported two cases of incomplete epidural analgesia in young children. In both, LES entry was identified by LOR with air. Both patients subsequently had epidurograms that revealed bubbles, presumed to be air-filled, posteriorly in the vertebral canal. Dalens thought the bubbles represented air injected with the LOR technique and considered they might explain the incomplete analgesia. Whether such considerations apply in parturients remains open to question, but common sense dictates that small air volumes be employed. Naulty et al[84] identified a 40% incidence of venous air embolism in healthy women undergoing epidural anesthesia, following injection of 5 mL of air with the LOR technique and recommended LOR with saline instead. Heggie[57] ascribes the occurrence of shoulder and neck pain during epidural anesthesia to injection of air into the epidural space during the LOR technique. Finally, Doughty[38] strongly advocates a 20-mL, saline-filled syringe, to elicit LOR on entry into the epidural space. He applies the ball of his index finger or palm of the right hand to the syringe plunger during advance of the Tuohy needle, while the force applied through the syringe barrel (with the left hand) propels the needle through the interspinous ligaments. Doughty considers this technique "almost dural puncture proof."

On balance, LOR with saline seems the preferred technique, although some anesthesiologists remain firm proponents of air, while ensuring that only a small volume enters the epidural space.

Test Dose

Mulroy[81] discusses test doses elsewhere in this issue. Controversy surrounds epinephrine-containing markers in labor, for three principal reasons: (1) pregnant women have a decreased response to the chronotropic effect of β-agonists[36]; (2) spontaneous maternal heart rate accelerations may occur in labor in response to contractions[16]; and (3) epinephrine may reduce uterine blood flow, an important concern in high-risk parturients.[61] Work by Eisenach's group suggests that 5 mL of 2% lidocaine,[96] or 2% chloroprocaine,[52] constitute effective test doses to exclude an intravascular catheter. Leighton and Gross[70] consider air an acceptable test dose, whereas others omit a test dose in labor altogether. Every anesthesiologist should heed Scott's[97] warning that "probably the most dangerous aspect of a false negative test dose is the confidence it inspires in the anaesthetist that all is well and the main dose can be injected with impunity." No single test of accidental subarachnoid/intravascular injection is 100% reliable, and every dose should be considered a test dose.

Intermittent Top-ups or Continuous Infusion?

Much print has been devoted to the virtues of CIEA, which some consider "state of the art" obstetric anesthesia.[20] Advantages claimed include smoother control of labor pain and lack of "roller-coaster" analgesia; less need for top-ups, with correspondingly reduced demand on medical and nursing staff; increased safety; and more stable cardiovascular parameters.[101] However, carefully designed studies do not consistently support these claims, although CIEA retains an important place in obstetric anesthesia.

Smedstad and Morison,[99] in a well-designed prospective study, compared CIEA with intermittent top-ups of 0.25% bupivacaine. All subjects received an initial injection of bupivacaine, 12 mL, in divided doses over 10 minutes. The CIEA group then received bupivacaine infusion, 8 mL/h, while the intermittent group had 8 mL as needed, when determined by their nurse. Pain relief and maternal satisfaction did not differ between groups. Mothers in the CIEA group received more bupivacaine than the intermittent group ($P < 0.01$) but maternal and umbilical cord levels remained low in both groups. More women in the CIEA group required outlet forceps delivery ($P < 0.05$), but midforceps and cesarean section rates proved similar in the two groups. Hicks et al,[58] in contrast, compared CIEA (0.075% bupvacaine, 12–18 mL/h) with intermittent top-ups of 0.5%. Parturients in the CIEA group had significantly better analgesia ($P < 0.025$), but these authors found no significant difference in the total bupivacaine dose administered. Neither did obstetric outcome differ. Bogod et al[9] randomly assigned primigravidae to receive CIEA 0.125% bupivacaine, 10 mL/h, plus top-ups if necessary, or intermittent 0.25% to 0.5% bupivacaine. The mean interval between top-ups proved significantly longer in the CIEA group (218 versus 152 minutes). However, as with Smedstad's study, women in the CIEA group received a higher mean bupivacaine dose (178 versus 103 mg). Subjects in the CIEA group demonstrated a higher incidence of motor block (64% versus 44%), but the authors found no difference in obstetric outcome. They concluded that CIEA probably increases patient satisfaction and gives better pain relief because of the increased interval between top-ups.

In Smedstad's study, the comparable first-stage pain relief may have been due to the timed top-ups. Purdy et al[90] prospectively studied women, during first-stage labor, who received bupivacaine 0.5%, 0.375%, or 0.25%, either by timed injections at 90-minute intervals, or on request when contractions became painful. In the 0.375% group, the authors found significantly better analgesia in patients having regular timed boluses, although they could not demonstrate this difference in the 0.25% and 0.5% recipients. Although a difficult study to interpret, its important message appears to be that regular (timed) top-ups will secure better pain relief. If anesthesiologists cannot ensure immediate availability of timed top-ups, I believe they should employ CIEA, to secure the best pain relief. However, an appropriate member of the anesthesia team must be immediately available to treat any adverse reaction in epidural anesthesia, and, in my view, CIEA cannot be justified for convenience, if convenience implies that the anesthesiologist is not immediately available.

Johnsrud et al[65] randomized nullipara to receive CIEA (bupivacaine, 0.25%, 7 mL/h) only in first-stage labor, or throughout first and second stage. Duration of second-stage labor was the same in both groups, although there were more persistent malrotations when CIEA was discontinued. However, the incidence of instrumental deliveries (25%) did not differ between groups. Chestnut's group[25] similarly randomized women to receive CIEA with 0.75% lidocaine throughout labor until delivery or saline administered by syringe substitution at 8 cm or more dilatation. Although analgesia tended to be better in the lidocaine group, duration of the second stage, and frequency of operative delivery were comparable. Both studies concluded that maintenance of CIEA did not prolong second-stage labor or affect obstetric outcome.

In summary, CIEA gives comparable, or better maternal pain relief, but at the price of increased motor block and greater doses of local anesthetic. Also, CIEA should be maintained throughout labor, including the second stage. Naulty[82] believes significantly more investigation must be undertaken to determine optimal drug, dose, and method of infusion, although many effective combinations have been employed (Table 1).

Opioids Added to Continuous Epidural Infusion

In the previously cited study by Chestnut et al,[23] CIEA (0.0625% bupivacaine plus fentanyl, 2 μg/mL) when compared with 0.125%

Table 1. CONTINUOUS INFUSION EPIDURAL ANALGESIA: SOME SUGGESTED REGIMENS

	Infusion		
Loading Dose	**Drugs**	**Dose mL/h**	**Comments**
Bupivacaine, 0.5%, 8–10 mL	Bupivacaine, 0.075%	15	Motor block + → + +
Bupivacaine, 0.25%, 10–15 mL	Bupivacaine, 0.125%–0.25%	8–20	Motor block + + with 0.25% infusion
Bupivacaine, 0.08%, 8–12 mL	Bupivacaine, 0.08%	25	Less hypotension; fewer high blocks
Bupivacaine, 0.125%, 16–20 mL Fentanyl, 100 μg	Bupivacaine, 0.0625%–0.125% Fentanyl 2 μg/mL	8–12	Excellent analgesia Pruritus +
Bupivacaine, 0.125%–0.25%, 8–10 mL Butorphanol, 0.2 mg/mL	Bupivacaine, 0.0625%–0.125% Butorphanol, 0.1 mg/mL	8–12	Sedation + – → +
Bupivacaine, 0.0625%–0.125%, 8–10 mL Sufentanil, 1–2 μg/mL	Bupivacaine, 0.03125%–0.0625% Sufentanil, 0.2–0.3 μg/mL	6–10	Ambulatory analgesia with 0.0312%
Bupivacaine, 0.125%–0.25%, 8–12 mL Meperidine, 25–50 mg	Bupivacaine, 0.125% Meperidine, 1 mg/mL	8–10	Pruritus minimal

bupivacaine alone, gave comparable first- and second-stage pain relief, but women who received bupivacaine alone were more likely to have motor block at full dilatation ($P < 0.001$). Celleno and Capogna[17] also found that addition of fentanyl, 2 μg/mL, to CIEA with 0.125% bupivacaine plus 1:800,000 epinephrine, produced excellent labor analgesia, with a reduced total bupivacaine dose (55 versus 109 mg). Phillips[87] randomly assigned laboring women to receive a bolus of 0.125% bupivacaine, plus sufentanil 2 μg/mL, followed 30 minutes later by CIEA with bupivacaine/sufentanil, or 0.25% bupivacaine, 10 to 15 mL, followed by plain bupivacaine infusion. Analgesia was significantly better in the bupivacaine/sufentanil group, and subjects required fewer top-ups and had less motor weakness. In summary, the addition of opioids to CIEA enables the use of more dilute local anesthetic concentrations, diminishes motor blockade, and reduces total bupivacaine dose, without affecting outcome. One hope for the future is that the combination of potent opioids and dilute local anesthetics (e.g., sufentanil, with bupivacaine, 0.0312%) will permit mothers to ambulate during labor.[83]

Patient-Controlled Epidural Analgesia

The widespread interest in intravenous patient-controlled analgesia (PCA) influenced some workers to explore similar techniques in women having LEA for labor. Gambling et al[47] undertook a randomized, single-blinded, placebo-controlled study of women who received epidural bupivacaine, 0.125%. Group A subjects had a background infusion of 4 mL/h, with bolus doses of 4 mL, self-administered, to a maximum of 16 mL/h. Group B subjects had a continuous infusion at 12 mL/h, through the same PCA apparatus with the demand button deactivated. Patients in the patient-controlled epidural analgesia (PCEA) group received significantly less local anesthetic (11 versus 15 mg/h) but had similar pain relief. Women expressed overall satisfaction with PCEA, appreciating control over their own pain relief. The same workers compared PCEA and conventional intermittent top-ups in nullipara during first-stage labor.[46] PCEA subjects self-administered bupivacaine, 0.125% plus 1:400,000 epinephrine, in 4-mL increments to a maximum of 12 mL/h, as required. Group B participants received 12 mL of 0.125% with epinephrine, on request. In both groups the maximum hourly dose of bupivacaine was limited to 15 mg. The study concluded when patients reached second-stage labor. Both groups had low hourly bupivacaine requirements (approximately 6 mg), and pain relief was similar. Patient satisfaction, again, proved to be higher in the PCEA group.

Lysak and colleagues[72] studied the efficacy of PCEA during labor, with three different solutions. Parturients were assigned to one of four groups, after establishment of the epidural block: (1) CIEA with bupivacaine, 0.125%; (2) PCEA, bupivacaine 0.125% (B); (3) PCEA, bupivacaine, 0.125%, plus fentanyl 1 μg/mL (BF); (4) PCEA, bupivacaine, 0.125%, plus 1:400,000 epinephrine, plus fentanyl, 1 μg/mL (BFE). At hourly intervals, the investigators studied blood pressure, heart rate, sensory level, motor strength, and recorded side effects such as pruritus, nausea, or respiratory depression. Women assessed their overall satisfaction with labor analgesia, on a four-point scale, presented on the first postpartum day. Compared with CIEA, PCEA with plain bupivacaine did not decrease local anesthetic usage or average hourly infusion rates. However, the addition of fentanyl in both groups (BF and BFE) decreased the administered hourly dose. Mild pruritus occurred in patients receiving fentanyl, and more frequent dense motor block in the BFE group. The authors considered PCEA safe and effective for labor analgesia, and, of the solutions used, 0.125% bupivacaine plus fentanyl, 1 μg/mL (BF), gave the best results.

ANESTHESIA FOR DELIVERY

Mothers delivering spontaneously, with the fetus occipitoanterior, need minimal additional delivery analgesia (e.g., perineal infiltration). For low forceps delivery, the epidural should be topped up with 10 to 15 mL of 0.25% bupivacaine or 1.5% lidocaine, for example. Trial-of-forceps procedure (or rotational forceps delivery) requires more extensive and profound block, e.g., lidocaine, 2% plus epinephrine 1:200,000, 15 to 20 mL.

COMPLICATIONS OF EPIDURAL ANALGESIA IN LABOR

Gutsche[55] discusses the complications of epidural block elsewhere, and the author refers the reader to that review for a more detailed discussion.

Maternal Hypotension

Maternal hypotension (systolic blood pressure < 100 mm Hg, or a $> 25\%$ decrease from the preepidural figure) needs immediate correction. Before epidural analgesia in labor, I preload mothers with Ringer's lactate solution, 10 to 15 mL/kg, and ensure they remain on the side (left, or right) or tilted by a firm pillow/wedge, throughout labor. Intravenous ephedrine, 10 to 15 mg, augmented lateral tilt, and mask O_2 remain the standby for hypotension, if it occurs despite these precautions.

Shivering

Shivering may follow induction of LEA, and its occurrence has been extensively investigated. Many factors may be involved, including cold "prep" solutions, intravenous fluids and local anesthetics, and redistribution of heat from the body core to outer shell. Recent work demonstrates that epidural sufentanil causes a dose-related decrease in maternal temperature, while also preventing shivering, in doses exceeding 50 μg.[97]

Inadvertent Dural Puncture

The quoted incidence of inadvertent dural puncture varies from 0.2% to more than 3%, although it should be less than 0.5%. In labor, the appropriate response is usually to withdraw the epidural needle and reinsert it at an adjacent interspace. Although caution demands that subsequent local anesthetic doses be carefully administered to avoid a high block, I have not found requirements diminished in these parturients. If the epidural catheter penetrates dura, the option exists to convert to continuous spinal analgesia. When inadvertent dural puncture occurs, I administer a prophylactic through-the-catheter epidural blood patch, as recommended by Cheek et al[19] and Gutsche,[54] before the patient leaves the recovery room. I inject 15 to 20 mL of autologous blood (obtained from the patient's antecubital fossa under full aseptic precautions) and keep the patient recumbent for 45 to 60 minutes thereafter. Colonna-Romano and Shapiro[29] prospectively randomized sequential parturients, with inadvertent wet-tap, to receive through-the-catheter prophylactic epidural blood patch, 15 mL of autologous blood, or conservative management with excess fluids, and delayed ambulation. All patients were followed for 4 days. Sixteen of 20 subjects in the control group developed postdural puncture headache, and seven eventually had an epidural blood patch. In the study group, 4 of 19 developed postdural puncture headache (21%), but were successfully treated with a second epidural blood patch. The difference in postdural puncture headache incidence between the two groups (21% vs 80%) was highly significant ($P < 0.005$). Ong et al[85] found that parturients who had a previous wet tap (with or without epidural blood patch) had a significantly lower incidence of successful block in their subsequent labor.

Total or High Spinal Block

Inadvertently high block may result from unintentional subarachnoid, and less frequently, subdural injection, of an epidural dose. Any individual giving obstetric LEA must be able and immediately available to treat this complication. The block usually regresses without neurologic complication, but cases of prolonged or permanent neurologic deficit have been reported. The preferred way to manage high block is prevention. Each dose through the catheter must be given in small increments (lidocaine, 50 mg; bupivacaine, 5–7 mg; chloroprocaine, 100 mg) followed by a wait of 3 to 5 minutes.[55]

CATHETER-RELATED COMPLICATIONS

Blood Vessel Puncture

Blood vessel puncture has an incidence of approximately 3% to 4%, although one recent study cited 11% with rigid multiorifice catheters.[5] Multiorifice catheters can function effectively, while also being in a vein (or even CSF), and aspiration may be negative because the blood vessel collapses around the catheter. Treatment of an intravascular catheter is simply to remove it and repeat the procedure. Other catheter-related complications such as shearing and knotting may occur, but can be avoided if the epidural catheter is inserted no more than 4 cm, and never withdrawn through the Tuohy needle.

Failed or Unsatisfactory Block

Failed or unsatisfactory blocks have an incidence of 1% when the initial injection is made through the needle, but 10% when made through the catheter.[55] Gutsche,[55] therefore, recommends initial injection through the needle, in incremental doses, before passing the catheter. Failure of catheter passage has a reported incidence of 0.5% to 4% and may indicate needle bevel impinging on dura, bevel against epidural vein or nerve root, bevel in the lateral, narrow aspect of the epidural space, bevel incompletely through ligamentum flavum, and needle not in the epidural space. Boezaart[8] described a 23-year-old primigravid woman, with a unilateral block from an epidural catheter inserted via a midline approach. Despite a second injection of bupivacaine, followed by 10 mL of lidocaine, 1%, with the patient positioned on her nonanalgesic left side, analgesia remained confined to the right side. He left the epidural catheter in situ and supplemented pain relief with intravenous meperidine. Following delivery, radiopaque dye was injected via the epidural catheter, and CT-epidurography performed. The dye confirmed a right paravertebral collection of contrast medium, and the CT scan showed a partition separating the LES into left and right compartments, both anteriorly and posteriorly. Boezaart discussed other possible causes for hemianalgesia including (1) patient positioned on one side; (2) congenital anterior and posterior midline partitions; (3) partial passage of the epidural catheter into the paravertebral space; and (4) lateral placement of the catheter. (In this case, he considered the partition, separating the LES into right and left compartments, an explanation for the inadequate block.)

Gutsche[55] calls unblocked segments "windows of absent analgesia," which can frequently be eliminated by "repainting the fence" with an additional dose of local anesthetic. One-sided blocks may be corrected by placing the patient in full lateral position, deficient side down, and reinjecting. Insertion of an epidural catheter more than 3 cm beyond the tip of the epidural needle increases the incidence of unsatisfactory block. It is never a sin to remove an epidural catheter and repeat the procedure, if the block is ineffective.

Postpartum Backache

Moir and Davidson[79] noted postpartum back pain in 38% of women delivering without LEA, compared with 22% of those who had an epidural. They suggested back pain resulted from stretching and flattening of the lumbar lordotic curve. Ensuring proper placement of a woman in the lithotomy position, with the hips supported, not hanging off the delivery table, and the lordotic curvature maintained with a small roll of sheets under the lumbar spine, will minimize backache.[55] In a review of more than 11,000 women, MacArthur et al[73] identified 14% who reported backache. Sixty-nine percent of these had experienced the symptom for over 1 year. The authors found a significant association between backache and LEA (RR = 1.8). Nineteen per cent of women who had LEA reported backache, compared with 10% of those who did not. The association was consistent for normal vaginal and emergency cesarean deliveries, but no excess backache occurred in patients undergoing elective cesarean section. The authors considered the relationship between backache and LEA probably causal and suggested it might result from effective analgesia combined with stressed posture during labor.

NEUROLOGIC COMPLICATIONS

Overall, the incidence of neurologic complications following LEA is extremely low. Patients may experience symptoms of nerve compression, with areas of paresthesiae, diminished sensation, and muscle weakness (from lateral popliteal nerve compression, for example.) Lateral femoral cutaneous nerve compression, by the inguinal ligament in the lithotomy position, may result from improper positioning. Sciatica, or lumbosacral trunk compression, caused by pressure of the fetal head or the application of forceps, may also occur, particularly in women with flat or platypelloid pelves.

Epidural abscess and epidural hematoma represent extremely rare complications of epidural block.

References

1. Abboud TK, Khoo SS, Miller F, et al: Maternal, fetal, and neonatal responses after epidural anaesthesia with bupivacaine, 2-chloroprocaine, or lidocaine. Anesth Analg 61:638–644, 1982

2. Abouleish EI, Hanley ES, Palmer SM: Can epidural fentanyl control autonomic hyperreflexia in a quadriplegic parturient? Anesth Analg 68:523–526, 1989
3. Atkinson RS, Rushman GB, Lee JA: A synopsis of anaesthesia, 10th ed. Bristol, John Wright, 1987
4. Bates RG, Helm CW, Duncan A, et al: Uterine activity in the second stage of labour and the effect of epidural analgesia. Br J Obstet Gynaecol 92:1246–1250, 1985
5. Beck H, Brasson H, Doehn M, et al: Epidural catheters of the multiorifice type: Dangers and complications. Acta Anaesthesiol Scand 30:549–555, 1986
6. Blomberg RG, Olsson SS: The lumbar epidural space in patients examined with epiduroscopy. Anesth Analg 68:157–160, 1989
7. Blomberg RG: Technical advantages of the paramedian approach for lumbar epidural puncture and catheter introduction. A study using epiduroscopy in autopsy subjects. Anaesthesia 43:837–843, 1988
8. Boezaart AP: Computerized axial tomo-epidurographic and radiographic documentation of unilateral epidural analgesia. Can J Anaesth 36:697–700, 1989
9. Bogod DG, Rosen M, Rees GA: Extradural infusion of 0.125% bupivacaine at 10 ml h^{-1} to women during labour. Br J Anaesth 59:325–330, 1987
10. Bonica JJ: Principles and Practice of Obstetric Analgesia and Anesthesia. Philadelphia, FA Davis, 1969
11. Brian JE, Clark RB, Quirk JG: Autonomic hyperreflexia, cesarean section and anesthesia. J Reprod Med 33:645–648, 1988
12. Bromage P: Epidural Analgesia. Philadelphia, Saunders, 1978
13. Brownridge P: Epidural bupivacaine-pethidine mixture. Clinical experience using a low-dose combination in labour. Aust NZ J Obstet Gynaecol 28:17–24, 1988
14. Carrie LE: Extradural, spinal or combined block for obstetric surgical anaesthesia. Br J Anaesth 65:225–233, 1990
15. Carrie LE: The paramedian approach to the epidural space. Anaesthesia 32:670–671, 1977
16. Cartwright B, McCarroll SM, Antzaka C: Maternal heart rate changes with a plain epidural test dose. Anesthesiology 65:226–228, 1986
17. Celleno D, Capogna G: Epidural fentanyl plus bupivacaine 0.125 per cent for labour: Analgesic effects. Can J Anaesth 35:375–378, 1988
18. Chater SN, Greig AJ, Sugden JC: Epidural anaesthesia in the presence of a cerebral tumour. Anaesthesia 42:433, 1987
19. Cheek TG, Banner R, Sauter J, et al: Prophylactic extradural blood patch is effective. Br J Anaesth 61:340–342, 1988
20. Cheek TG, Gutsche BB: Epidural analgesia for labor and vaginal delivery. Clin Obstet Gynecol 30:515–529, 1987
21. Chestnut DH, Laszewski LJ, Pollack KL, et al: Continuous epidural infusion of 0.0625% bupivacaine-0.0002% fentanyl during the second stage of labor. Anesthesiology 72:613–618, 1990
22. Chestnut DH, Geiger M, Bates JN, et al: The influence of pH-adjusted 2-chloroprocaine on the quality and duration of subsequent epidural bupivacaine analgesia during labor: A randomized double-blind study. Anesthesiology 70:437–441, 1989
23. Chestnut DH, Owen CL, Bates JN, et al: Continuous infusion epidural analgesia during labor: A randomized double-blind comparison of 0.0625% bupivacaine/0.0002% fentanyl versus 0.125% bupivacaine. Anesthesiology 68:754–759, 1988
24. Chestnut DH, Vandewalker GE, Owen CL, et al: The influence of continuous epidural bupivacaine analgesia on the second stage of labor and method of delivery in nulliparous women. Anesthesiology 66:774–780, 1987
25. Chestnut DH, Bates JN, Choi WW: Continuous infusion epidural analgesia with lidocaine: Efficacy and influence during the second stage of labor. Obstet Gynecol 69:323–327, 1987
26. Cleland JG: Continuous paradural and caudal block in obstetrics and surgery with postoperative analgesia. Anesth Analg 31:289–301, 1952
27. Cleland JG: Paravertebral anesthesia in obstetrics, experimental and clinical basis. Surg Gynecol Obstet 57:51–62, 1933
28. Cohen SE, Tan S, Albright GA, et al: Epidural fentanyl/bupivacaine mixtures for obstetric analgesia. Anesthesiology 67:403–407, 1987

29. Colonna-Romano P, Shapiro BE: Unintentional dural puncture and prophylactic epidural blood patch in obstetrics. Anesth Analg 69:522–523, 1989
30. Curbelo MM: Continuous paradural segmental anesthesia by means of a ureteral catheter. Anesth Analg 28:13–22, 1949
31. Curelaru I, Sander L: Eugen Bogdan Aburel (1899–1975). The pioneer of regional analgesia for pain relief in childbirth. Anaesthesia 37:663–669, 1982
32. Dalens B, Bazin J-E, Haberer J-P: Epidural bubbles as a cause of incomplete analgesia during epidural anesthesia. Anesth Analg 66:679–683, 1987
33. Datta S, Lambert DH, Gregus J, et al: Differential sensitivities of mammalian nerve fibers during pregnancy. Anesth Analg 62:1070–1072, 1983
34. David H, Rosen M: Perinatal mortality after epidural analgesia. Anaesthesia 31:1054–1059, 1976
35. Deckardt R, Fernbacher PM, Schneider KT, et al: Maternal oxygen saturation during labor and delivery: Pain dependent alterations and effects on the newborn. Obstet Gynecol 70:21–25, 1987
36. De Simone CA, Leighton BL, Norris MC, et al: The chronotropic effect of isoproterenol is reduced in term pregnant women: Anesthesiology 69:626–628, 1988
37. DiFazio CA, Carron H, Grosseignt KR, et al: Comparison of pH-adjusted lidocaine solutions for epidural anaesthesia. Anesth Analg 65:760–764, 1986
38. Doughty A: Correspondence. Anaesthesia 37:470, 1982
39. Doughty A: Selective epidural analgesia and the forceps rate. Br J Anaesth 41:1058–1062, 1969
40. Eisenach JC, Grice SC, Dewan DM: Epinephrine enhances analgesia produced by epidural bupivacaine during labor. Anesth Analg 66:447–451, 1987
41. Elsenstein S: The trefoil configuration of the lumbar vertebral canal. J Bone Joint Surg 62B:73–77, 1980
42. Finer P, Blair J, Rowe P: Epidural analgesia in the management of labor pain and sickle-cell crisis—A case report. Anesthesiology 68:799–800, 1988
43. Flowers CE, Hellman LM, Hingson RA: Continuous peridural anesthesia for labor, delivery and cesarean section. Anesth Analg 28:181–189, 1949
44. Flynn RJ, McMurray TJ, Dwyer R, et al: Comparison of plasma bupivacaine concentrations during continuous extradural infusion for labour. Br J Anaesth 61:382–384, 1988
45. Fusi L, Steer PJ, Maresh MJ, et al: Maternal pyrexia associated with the use of epidural analgesia in labour. Lancet 1:1250–1252, 1989
46. Gambling DR, McMorland GH, Yu P, et al: Comparison of patient-controlled epidural analgesia and conventional intermittent "top-up" injections during labour. Anesth Analg 70:256–261, 1990
47. Gambling DR, Yu P, McMorland GH, et al: A comparative study of patient controlled epidural analgesia (PCEA) and continuous infusion epidural analgesia (CIEA) during labour. Can J Anaesth 35:249–254, 1988
48. Gaynor A: The lumbar epidural region: anatomy and approach. *In* Reynolds F (ed): Epidural and Spinal Blockade in Obstetrics. Philadelphia, Bailliere Tindall, 1990, pp 3–18
49. Goodfellow CF, Hull MG, Swaab DF, et al: Oxytocin deficiency at delivery with epidural analgesia. Br J Obstet Gynaecol 90:214–219, 1983
50. Grice SC, Eisenach JC, Dewan DM: Labor analgesia with epidural bupivacaine plus fentanyl: Enhancement with epinephrine and inhibition with 2-chloroprocaine. Anesthesiology 72:623–628, 1990
51. Grice SC, Eisenach JC, Dewan DM, et al: Evaluation of informed consent for anesthesia for labor and delivery. Anesthesiology 69:A664, 1988
52. Grice SC, Eisenach JC, Dewan DM, et al: Evaluation of 2-chloroprocaine as an effective test dose for epidural analgesia. Anesthesiology 67:A627, 1987
53. Griffin RM, Scott RP: A comparison between the midline and paramedian approaches to the extradural space. Anaesthesia 39:584–586, 1984
54. Gutsche BB: Lumbar epidural analgesia in obstetrics: Taps and patches. *In* Reynolds F (ed): Epidural and Spinal Blockade in Obstetrics. Philadelphia, Bailliere Tindall, 1990, pp 95–106
55. Gutsche BB: Complications of regional anesthesia in obstetrics. 38th Annual

Refresher Course Lectures. Chicago, American Society of Anesthesiologists, 1987, p 173
56. Harrison GR, Clowes NW: The depth of the lumbar epidural space from the skin. Anaesthesia 40:685–687, 1985
57. Heggie NM: Unexplained pain during epidural anaesthesia. Anaesthesia 39:609–610, 1984
58. Hicks JA, Jenkins JG, Newton MC, et al: Continuous epidural infusion of 0.075% bupivacaine for pain relief in labour. Anaesthesia 43:289–292, 1988
59. Hingson RA, Southworth JL: Continuous paradural anesthesia. Anesth Analg 23:215–217, 1944
60. Hingson RA, Edwards WB: Continuous caudal analgesia; an analysis of the first 10,000 confinements thus managed with the report of the authors' first 1000 cases. JAMA 23:538–546, 1943
61. Hood DD, Dewan DM, James FM: Maternal and fetal effects of epinephrine in gravid ewes. Anesthesiology 64:610–613, 1986
62. Hughes AB, Devoe LD, Wakefield ML, et al: The effects of epidural anesthesia on the doppler velocimetry of umbilical and uterine arteries in normal term labor. Obstet Gynecol 75:809–812, 1990
63. Hunt CO, Naulty JS, Malinow AM, et al: Epidural butorphanol-bupivacaine for analgesia during labor and delivery. Anesth Analg 68:323–327, 1989
64. Janbu T: Blood velocities in the dorsalis pedis and radial arteries during labour. Br J Obstet Gynaecol 96:70–79, 1989
65. Johnsrud M-L, Dale PO, Lovland B: Benefits of continuous infusion epidural analgesia throughout vaginal delivery. Acta Obstet Gynecol Scand 67:355–358, 1988
66. Jones G, Paul DL, Alton RA, et al: Comparison of bupivacaine and bupivacaine with fentanyl in continuous extradural analgesia during labour. Br J Anaesth 63:254–259, 1989
67. Justins DM, Knott C, Luthman J, et al: Epidural versus intramuscular fentanyl. Analgesia and pharmacokinetics in labour. Anaesthesia 38:937–942, 1983
68. Justins DM, Francis D, Houlton PG, et al: A controlled trial of extradural fentanyl in labour. Br J Anaesth 54:409–414, 1982
69. Knapp RM: Legal view of informed consent for anesthesia during labor. Anesthesiology 72:211, 1990
70. Leighton BL, Gross JB: Air: An effective indication of intravenously located epidural catheters. Anesthesiology 71:848–851, 1989
71. Lirzin JD, Jacquinot P, Daillard P, et al: Controlled trial of extradural bupivacaine with fentanyl, morphine or placebo, for pain relief in labour. Br J Anaesth 62:641–644, 1989
72. Lysak SZ, Eisenach JC, Dobson CE: Patient-controlled epidural analgesia during labor: A comparison of three solutions with a continuous infusion control. Anesthesiology 72:44–49, 1990
73. MacArthur C, Lewis M, Knox EG, et al: Epidural anaesthesia and long term backache after childbirth. Br Med J 301:9–12, 1990
74. Macdonald R: Indications and contraindications for epidural blockade in obstetrics. *In* Reynolds F (ed): Epidural and spinal blockade in obstetrics. Philadelphia, Bailliere Tindall, 1990, pp 19–32
75. Maresh M, Choong K-H, Beard RW: Delayed pushing with lumbar epidural analgesia in labour. Br J Obstet Gynaecol 90:623–627, 1983
76. McMorland GH, Douglas MH, Jeffrey WK, et al: Effect of pH-adjustment of bupivacaine on onset and duration of epidural analgesia in parturients. Can Anaesth Soc J 33:537–541, 1986
77. Michael S, Richmond MN, Birks RJ: A comparison between open-end (single hole) and closed-end (three lateral holes) epidural catheters. Anaesthesia 44:578–580, 1989
78. Minnich ME, Quirk JG, Clark RB: Epidural anesthesia for vaginal delivery in a patient with idiopathic hypertrophic subaortic stenosis. Anesthesiology 67:590–592, 1987
79. Moir DD, Davidson S: Postpartum complications of forceps deliveries performed under epidural and pudendal nerve block. Br J Anaesth 44:1197–1199, 1972
80. Morgan BM, Bulpitt CJ, Clifton P, et al: Effectiveness of pain relief in labour: A survey of 1000 mothers. Br Med J 285:689–690, 1982

81. Mulroy MF: Epidural test dose. Clin Anaesthesiol 10:45–58, 1992
82. Naulty JS: Continuous infusions of local anesthetics and narcotics for epidural analgesia in the management of labor. Int Anesthesiol Clin 28:17–24, 1990
83. Naulty JS, Ross R, Bergen W: Epidural sufentanil-bupivacaine for analgesia during labor and delivery. Anesthesiology 71:A842, 1989
84. Naulty JS, Ostheimer GW, Datta S, et al: Incidence of venous air embolism during epidural catheter insertion. Anesthesiology 57:410–412, 1982
85. Ong BY, Graham CR, Ringaert KR, et al: Impaired epidural analgesia after dural puncture with and without subsequent blood patch. Anesth Analg 70:76–79, 1990
86. Philipson P, Jensen N-H: Maternal opinion about analgesia in labour and delivery. A comparison of epidural blockade and intramuscular pethidine. Eur J Obstet Gynaecol Reprod Biol 34:205–210, 1990
87. Phillips G: Continuous infusion epidural analgesia in labor: The effect of adding sufentanil to 0.125% bupivacaine. Anesth Analg 67:462–465, 1988
88. Phillips GH: Epidural sufentanil/bupivacaine combinations for analgesia during labor: Effect of varying sufentanil doses. Anesthesiology 67:835–838, 1987
89. Power I, Thorburn J: Differential flow from multi-hole epidural catheters. Anaesthesia 43:876–878, 1988
90. Purdy G, Curry J, Owen H: Continuous extradural analgesia in labour. Comparison between "on demand" and regular "top-up" injections. Br J Anaesth 59:319–324, 1987
91. Reynolds F, Laishley R, Morgan B, et al: Effect of time and adrenaline on the feto-maternal distribution of bupivacaine. Br J Anaesth 62:509–514, 1989
92. Reynolds F, O'Sullivan G: Epidural fentanyl and perineal pain in labour. Anaesthesia 44:341–344, 1989
93. Reynolds F: Epidural anaesthesia in obstetrics. Pros and cons for mother and baby. Br Med J 299:751–752, 1989
94. Robinson DE, Leicht CH: Epidural analgesia with low-dose bupivacaine and fentanyl for labor and delivery in a parturient with severe pulmonary hypertension. Anesthesiology 68:285–288, 1988
95. Roetman KJ, Eisenach JC: Evaluation of lidocaine as an intravenous test dose for epidural anesthesia. Anesthesiology 69:A669, 1988
96. Saunders NJ, Spiby H, Gilbert L, et al: Oxytocin infusion during second stage of labour in primiparous women using epidural analgesia: A randomised double blind placebo controlled trial. Br Med J 299:1423–1426, 1989
97. Scott DB: Test doses in extradural block. Br J Anaesth 61:129–130, 1988
98. Sevarino FB, Johnson MD, Lema MJ, et al: The effect of epidural sufentanil on shivering and body temperature in the parturient. Anesth Analg 68:530–533, 1989
99. Smedstad KG, Morison DH: A comparative study of continuous and intermittent epidural analgesia for labour and delivery. Can J Anaesth 35:234–241, 1988
100. Studd JW, Crawford JS, Duignan NM: The effect of lumbar epidural analgesia on the rate of cervical dilatation and the outcome of labour of spontaneous onset. Br J Obstet Gynaecol 87:1015–1021, 1980
101. Taylor HJ: Clinical experience with continuous epidural infusion of bupivacaine at 6 ml per hour in obstetrics. Can Anaesth Soc J 30:277–285, 1983
102. Thorp JA, Parisi VM, Boylan PC, et al: The effect of continuous epidural analgesia on cesarean section for dystocia in nulliparous women. Am J Obstet Gynecol 161:670–675, 1989
103. van Steenberge A, DeBroux HC, Noorduin H: Extradural bupivacaine with sufentanil for vaginal delivery. A double-blind trial. Br J Anaesth 59:1518–1522, 1987
104. Yarnell RW: A portable anaesthetic monitoring trolley for labour room placement of epidurals. Can J Anaesth 36:731–732, 1989

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CONTINUOUS SPINAL ANESTHESIA

Donald H. Lambert, PhD, MD

Dean[6] performed the first continuous spinal anesthetic in 1907 by leaving the spinal needle in place during the operation. In 1940, Lemmon[18] introduced the malleable needle and split mattress technique to overcome problems of needle trauma and breakage. Tuohy,[27] in 1944, was the first to use a spinal catheter; a no. 4 ureteral catheter inserted through a 15-gauge needle. Since then, the diameter of the needles and catheters has decreased (Table 1). Although continuous spinal anesthesia is useful,[8, 25] it has not gained the popularity of continuous epidural anesthesia.[20] This is because of the high incidence of spinal headache from the large needles required to insert the catheter.

ADVANTAGES AND DISADVANTAGES

Continuous spinal anesthesia has advantages over continuous epidural blockade[26]: (1) the visualization of CSF flow increases success; and (2) it requires 10 to 15 times less local anesthetic than epidural blockade, eliminating systemic toxic reactions. Continuous spinal anesthesia also has advantages over single-dose spinal anesthesia: (1) anesthesia can be prolonged indefinitely; (2) it may be given after patient positioning and with careful titration, minimizing cardiovascular instability; (3) using low doses of short-acting local anesthetics (procaine and lidocaine) shortens the recovery period; (4) prior placement of the catheter expedites the surgical schedule; and (5) subarachnoid narcotics may be administered for long-lasting postoperative analgesia.

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ANESTHESIOLOGY CLINICS OF NORTH AMERICA

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Table 1. CATHETERS

Type	Material	Gauge	Needle	Manufacturer
Epidural	Nylon, Teflon	19, 20	17, 18	Many
Spinal	Polyethylene	24	20, 21*	CSI
Pediatric epidural	Polyurethane	24	20	Preferred Medical
Spinal	Polyurethane	27	22	Preferred Medical
Spinal	Nylon	28	22	Concord Portex
Spinal	Nylon	28	22	Kendall
Spinal	Polyimide	28	22	Rusch
Spinal	Polyimide	32	26, 27	Rusch

*Special needles.

Disadvantages of continuous spinal anesthesia include (1) the additional time required for catheter placement, which occasionally proves difficult or impossible; (2) the high incidence of headache that occurs when large-diameter needles are used to insert large-diameter catheters; and (3) the potential for infection, nerve injury, and hemorrhage.

INDICATIONS AND CONTRAINDICATIONS

The indications and contraindications for continuous spinal anesthesia are the same as for single-injection spinal anesthesia. However, continuous spinal anesthesia is particularly useful (1) for critically ill patients for whom slow incremental dosing minimizes hemodynamic changes; (2) whenever the duration of the operation might exceed the duration of the single-injection technique; and (3) for potentially short operations where the flexibility of intermittent injections allows limiting the initial dose or using short-acting local anesthetics to shorten the recovery.

CATHETER PLACEMENT

Although most anesthesiologists are familiar with lumbar puncture, single-injection spinal anesthesia, and epidural anesthesia, the following is a brief outline for subarachnoid catheter placement. After lumbar puncture with an appropriate diameter needle, advance the spinal catheter through the needle. The 27-, 28-, and 32-gauge catheters require placing a special threading aid in the hub of the needle to guide and stiffen the catheter as it passes through the hub (Fig. 1). Resistance may be felt as the catheter passes through the tip of the needle. Markings on the catheter aid in estimating the distance the catheter has passed beyond the tip of the needle. Inserting the catheter 2 to 3 cm is sufficient.

After the catheter is inserted, the needle is slowly withdrawn over

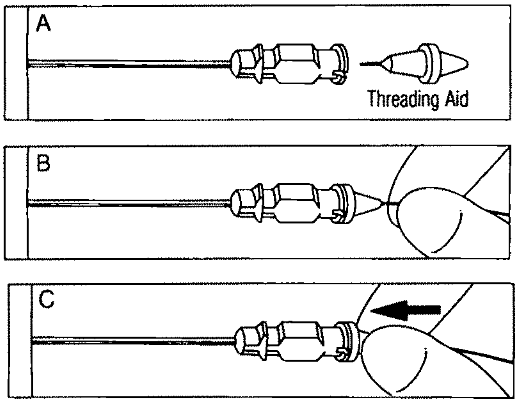

Figure 1. Method of inserting the smaller continuous spinal catheters. *A*, A threading aid is inserted into the needle hub to stiffen the catheter as it transitions the hub of the needle. *B*, When inserting the catheter with a permanent stylet, the catheter should be held close to the threading aid. *C*, Gentle forward pressure is exerted as the fingers slide up and over the introducer.

the catheter with one hand, while the other hand applies gentle inward pressure on the catheter to ensure that it is not withdrawn with the needle. Aspiration of CSF through the 19- to 28-gauge catheters shows proper placement. Although it is usually not possible to obtain CSF through the 32-gauge catheter, easy insertion and the development of anesthesia after local anesthetic injection signify proper placement of this catheter.

After the needle is withdrawn, make a loop with the catheter where it enters the skin and tape it up the patient's back to the shoulder, so that injections can be made from the head of the operating table. Attach a syringe adapter and syringe to the free end of the catheter.

One problem with continuous spinal anesthesia is the inability to thread the catheter into the CSF despite abundant CSF return. This occurs in roughly 5% to 15% of insertions. The reason is not precisely known, but it is not due to size because it occurs with all catheters. With the larger, long bevel, 17- or 18-gauge Tuohy needles, it is possible that the bevel only partially penetrates the dura (Fig. 2*A*). This allows abundant CSF return, but obstruction by the dura and arachnoid may prevent the catheter from entering the CSF (Fig. 2*B*). With the smaller, shorter, beveled spinal needles, the inability to thread probably is due to the catheter hitting the anterior wall of the dural sac (Fig. 3). If the spinal needle is central in the CSF and distant from the anterior wall of the dural sac (Fig. 4), the catheter will thread easily.

LOCAL ANESTHETICS AND INTRATHECAL OPIOIDS

Any of the local anesthetics or intrathecal opiates used for single-injection spinal anesthesia may be used for continuous spinal anesthesia. Yet, an advantage of continuous spinal anesthesia is the ability to tailor the duration of anesthesia to the length of operation. Procaine

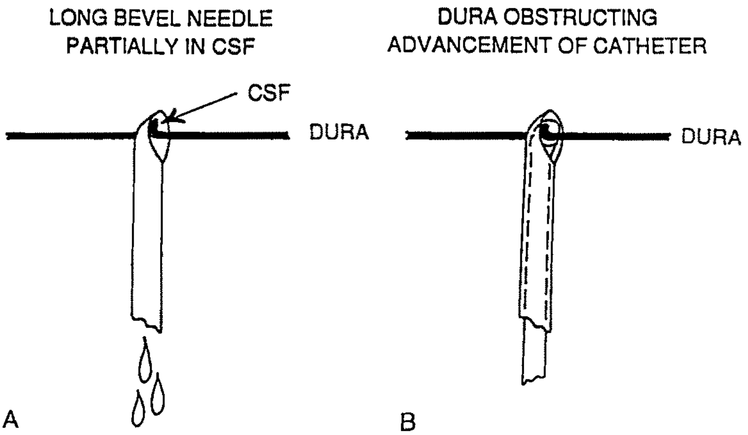

Figure 2. Failure to thread with the long bevel 17- or 18-gauge Tuohy needle. *A*, The bevel only partially penetrates the dura, allowing abundant CSF return. *B*, Dura and arachnoid prevent the catheter from entering the CSF.

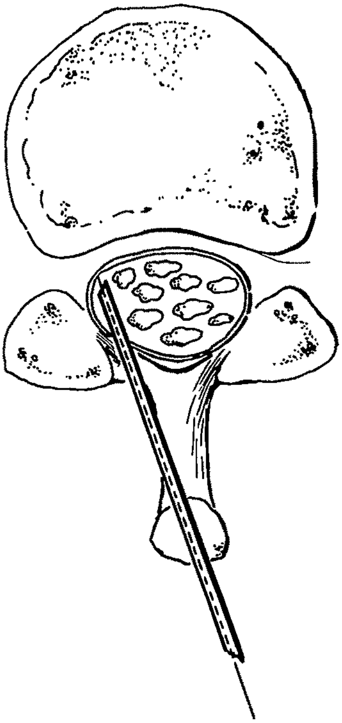

Figure 3. Inability to thread with the smaller shorter-beveled spinal needle. A possible cause is the catheter hitting the anterior wall of the dural sac.

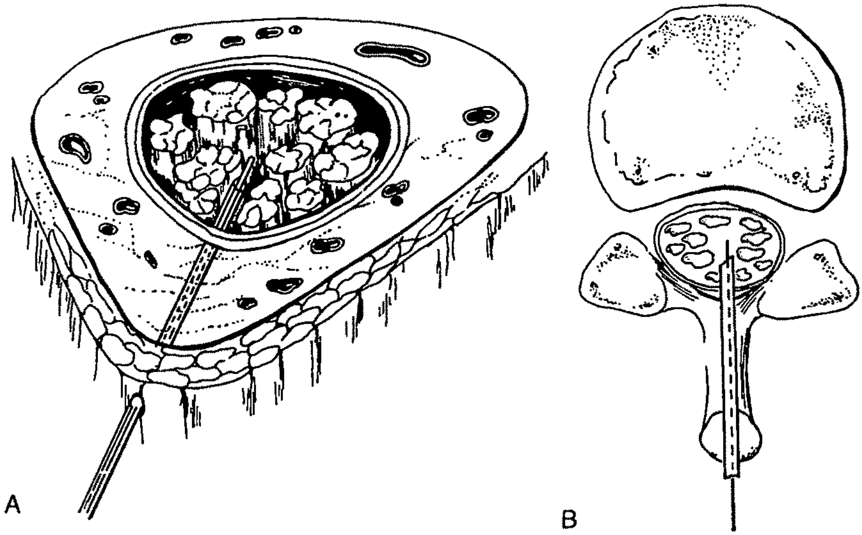

Figure 4. Optimum position of the spinal needle for threading a continuous spinal catheter. The spinal needle is centrally located (*A*) and distant from the anterior wall of the dural sac (*B*).

and lidocaine are particularly useful in this regard. Their short action minimizes the duration of any untoward hemodynamic changes and shortens recovery from anesthesia. After spinal anesthesia is achieved, repeat doses (20–25 mg) are administered when the patient notes any discomfort in the area of the incision. Reinjection causes prompt anesthesia, and it is not necessary to anticipate regression of anesthesia. Reinjecting when discomfort occurs ensures that the local anesthetic will not accumulate and that anesthesia will recede quickly after the operation. Twenty to 25 mg of lidocaine will last approximately 30 minutes. For long operations, 5-mg doses of bupivacaine or tetracaine (duration, 30–60 minutes) may be used to decrease the redosing frequency.

NEWER SMALL-GAUGE CATHETERS

Table 1 shows the many spinal catheters available and the needle size used to insert them. Despite lack of controlled data, the 32-gauge catheter appears useful for patients at high risk for developing spinal headache (very young patients, parturients) and the 27- or 28-gauge catheter for patients at lower risk (>50 years of age). For patients over 60 years of age, the size of the catheter is not as important because they infrequently develop spinal headache (SHA) and the large-diameter catheters that are easier to insert may be used.

THE 32-GAUGE CATHETER

A number of problems have emerged as the diameter of spinal catheters has decreased (Table 2). A disadvantage of the 32-gauge catheter is that it is not possible to aspirate CSF to verify proper position. Despite this, the 32-gauge catheter usually functions well if it threads easily during insertion. Another problem with the 32-gauge catheter is difficulty threading it into the subarachnoid space. This relates to its unique construction—a polyimide tube with an embedded stainless steel stylet that remains in place after insertion. This design is necessary to prevent kinking after insertion. However, if the stainless steel stylet bends during insertion, it is impossible to straighten it, and the needle cannot be removed without also pulling the catheter out. Therefore, this catheter needs to be handled gently to prevent bending while inserting it. When resistance to advancing the 32-gauge catheter occurs, only gentle pressure should be applied while holding the catheter close to the needle hub and threading aid (Fig. 1) to prevent bending. If bending appears imminent, try withdrawing the needle slightly while advancing the catheter. If this fails, the needle and catheter should be withdrawn and the procedure repeated at another interspace.

Instances of inadequate anesthesia may occur when small-gauge catheters are used.[12] This could be due to trapping or "sequestering" the catheter between the cauda equina nerves, so that the distribution of the local anesthetic is nonuniform (Fig. 5). Another possibility is that instead of being positioned cephalad and at the peak of the lumbar lordosis (Fig. 6), the catheter tip is located "too low" in the intrathecal space (Fig. 7). In the latter case, pooling of hyperbaric local anesthetic solution is likely and inadequate anesthesia possible. When this happens, instead of injecting more local anesthetic, it is preferable to increase the level of anesthesia by changing the baricity of the local anesthetic and patient position (e.g., isobaric or hypobaric solutions have the advantage of better distribution; see following).

COMPLICATIONS

Insertion of spinal catheters is simple and safe, yet complications occur. These include knotting[1] or breakage[12] of the catheter and

Table 2. PROBLEMS ASSOCIATED WITH THE 32-GAUGE CATHETER

1. Inability to aspirate CSF
2. Inability to thread into CSF
3. Kinking at the needle hub on insertion
4. Inadequate anesthesia
5. Broken catheters

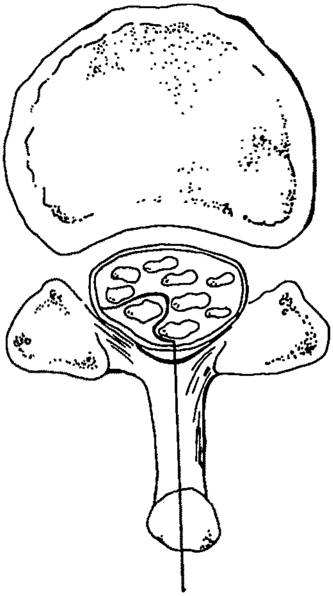

Figure 5. Inadequate anesthesia may be due to trapping or "sequestering" the catheter between the cauda equina nerves so that the distribution of the local anesthetic is nonuniform. An alternate explanation is shown in Figure 7.

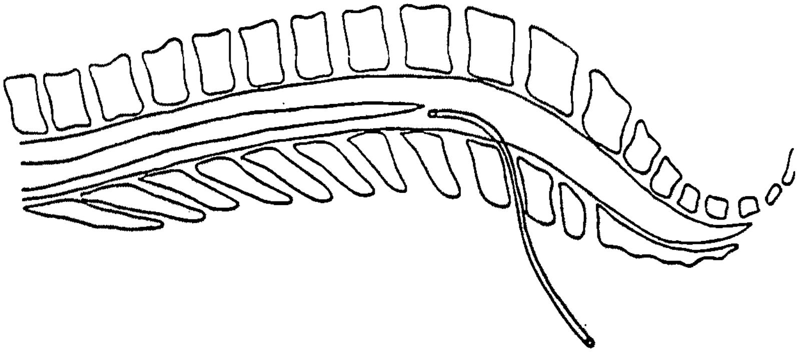

Figure 6. Ideal catheter location. The catheter courses cephalad with its tip at the peak of the lumbar lordosis.

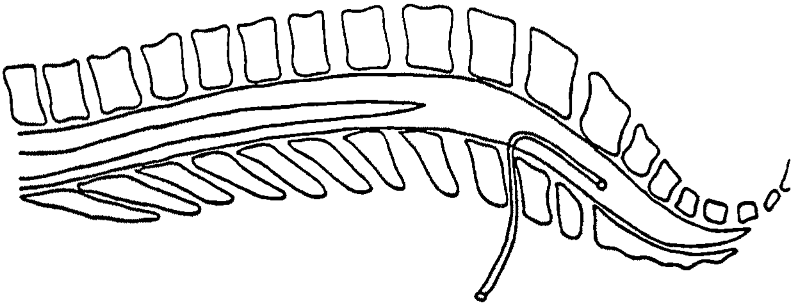

Figure 7. Catheter positioned too low in the intrathecal space. This leads to inability to achieve an adequate level of anesthesia because the local anesthetic pools in the distal end to the dural sac.

accidental removal or migration, resulting in anesthetic failure. Catheters can be inserted directly into a blood vessel. Lack of blood return on aspiration is no guarantee that the catheter is not in a blood vessel. However, the amount of local anesthetic used with spinal anesthesia is so small that accidental intravascular injection is benign.

Uncommonly, a catheter will knot. This is due to inserting excessive amounts of catheter.[1] Therefore, insert no more than 2 to 3 cm. Catheters can be sheared off when pulled backward through the needle.[15] When advancement is impossible, the needle and catheter should be withdrawn together, and the procedure repeated. Table 3 shows the break strength of the spinal catheters.[14, 29] Except for the polyimide catheters, all catheters elongate before breaking. When elongation occurs, this shows that the catheter is about to break. On the other hand, the polyimide catheters do not elongate and snap without warning. Therefore, it is important to handle the smaller catheters with care, especially when moving the patient and during removal. If the catheter does not come out easily during removal, the patient should be turned to the lateral decubitus position and the lumbar spine maximally flexed. This stretches the interspinous ligaments and reduces the "binding" action of the ligament on the catheter. If flexing the spine does not release the tension, then try other positions. A position will be found that will allow the catheter to be removed easily.

If a catheter is sheared or broken, no attempt should be made to retrieve the fragment unless it causes morbidity.[12] Inform the patient of what has happened and advise that this is rarely a problem. To date, approximately 10 to 15 catheters (27–32 gauge) have broken. A broken catheter likely remains lodged in the dura, ligamentum flavum, and interspinous ligament. Therefore, there is little chance of migration, and so far no patient has suffered any morbidity.[12]

SPINAL HEADACHE

Until recently, large-diameter needles were required to insert catheters for continuous spinal anesthesia, and the method was only used

Table 3. CATHETER BREAK STRENGTH

Manufacturer	Catheter Material	Gauge	Break Strength (lbs)	Elongation* (%)
Rusch	Teflon	20	3.0	280†
Rusch	Nylon	20	3.9	290†
Rusch	Polyimide	32	2.5	1, 100‡
Rusch	Polyimide	28	7.4	1, 100‡
Kendall	Nylon	28	1.25	550
Preferred Medical	Polyurethane	27	1.30	475

*Elongation of 1-inch length of catheter before breaking.
†Epidural catheter.
‡Stylet elongates 1%; polyimide elongates 100%.

in older patients believed to be at low risk for SHA. The incidence of SHA is due to the gauge of the needle (used to insert the catheter) (Fig. 8) and the age of the patient (Fig. 9).[28] The 32-gauge spinal catheter, which can be inserted through a 26-gauge needle, was designed for use in young patients who are prone to develop SHA. Still, Denny et al[7] prospectively observed only one SHA (in a 29-year-old man) out of 117 continuous spinal anesthetics done with an 18-gauge needle. They postulate that dural edema and inflammation from catheter irritation seals the dural puncture, decreases leakage of CSF, and prevents SHA. However, the average age of their patients was 63 years, with 66% over age 60. Based on this study, the need for smaller catheters has been questioned.[24] Yet, the low incidence of SHA observed by Denny et al[7] is not apparent from other investigations (Table 4). For example, Chen et al[3] observed a 36% incidence of SHA when 20-gauge catheters were introduced through an 18-gauge needle. All of the SHAs occurred in patients 18 to 53 years of age. There were no SHAs in patients over 60 years of age (Table 5). These data indicate that SHA occurring after continuous spinal anesthesia relates to the size of the needle used to insert the catheter.[14]

CAUDA EQUINA SYNDROME

Recently, Kendall Healthcare Products Company (Mansfield, MA) issued a precaution for continuous spinal anesthesia when using the

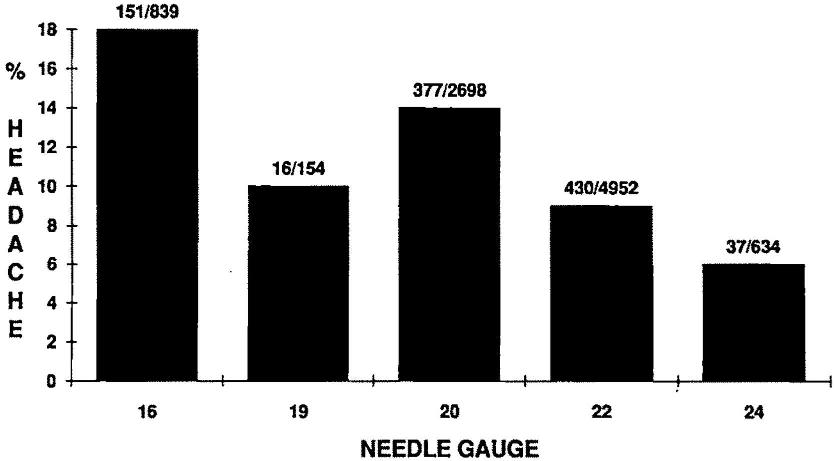

Figure 8. The incidence of spinal headache is related to the gauge of the spinal needle used for lumbar puncture. The ratio above each bar is the number of headaches to the total number of spinal anesthetics given with that gauge needle. (*Data from* Vandam LD, Dripps RD: Long-term follow-up of patients who received 10,098 spinal anesthetics: Syndrome of decreased intracranial pressure (headache and ocular and auditory difficulties). JAMA 161:586–591, 1956.)

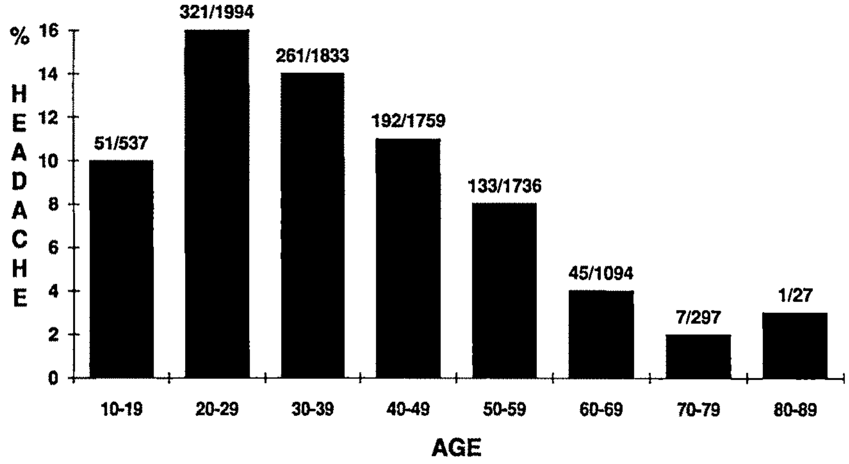

Figure 9. The incidence of spinal headache is a function of age. The ratio above each bar is the number of headaches to the total number of spinal anesthetics given to that age group. (*Data from* Vandam LD, Dripps RD: Long-term follow-up of patients who received 10,098 spinal anesthetics: Syndrome of decreased intracranial pressure (headache and ocular and auditory difficulties). JAMA 161:586–591, 1956.)

Table 4. INCIDENCE OF HEADACHE WITH CONTINUOUS SPINAL ANESTHESIA

Author	Year	Gauge	% Headache	Reference
Lemmon	1940	17, 18, 19	2.5	18
Tuohy	1945	15	3–5	27
Cann	1948	15	30	2
Kallos	1972	18	0	16
Giuffrida	1972	20, 21	16*	10
Peterson	1983	18	0	22
Denny	1987	18	1	7
Winnie	1988	17, 18, 20, 21	0	Unpublished
Cohen	1989	17	20*	4
Gold	1989	18	12	11
Culling	1989	18	22	5
Hurley	1990	26	4	12
Norris	1990	17	54*	21
Chen	1990	18	36*	3

*Pregnant patients.

Table 5. SPINAL HEADACHE AND CONTINUOUS SPINAL ANESTHESIA

	SHA*	Percent
Overall	5/14	36
Age, 18–53	5/5	100
Age, 61–82	0/9	0

*Number of SHA/total number continuous spinal anesthetics.

Data from Chen L, Fitzgerald TE, Miller FL, et al: Post dural puncture headache and continuous spinal anesthesia. Reg Anaesth 15:268, 1990.

28-gauge Cospan spinal catheter (Kendall Healthcare Products Company letter to Chiefs of Anesthesia Departments). The Kendall Company received several reports of neurologic deficits associated with continuous spinal anesthesia that were characterized by perineal sensory loss and changes in sphincter function. Review of these reports indicated the following similarities: (1) the use of 5% lidocaine (50 mg/mL) in 7.5% dextrose; (2) less than the expected anesthetic effect for a given dose; (3) an initial lidocaine dosage of 100 mg or more to establish the spinal anesthetic; and (4) a total lidocaine dosage exceeding 100 mg.

The Kendall Company issued the following recommendations to reduce the risk of these complications: (1) not threading the spinal catheter more than 2 cm beyond the tip of the needle; (2) limiting the use of 5% lidocaine in 7.5% dextrose to 100 mg in establishing the initial block; (3) using less concentrated local anesthetic; and (4) limiting the total dose of drug administered in a manner consistent with the duration of the operation.

A possible mechanism for these neurologic deficits is maldistribution of 5% lidocaine in 7.5% dextrose (see previous discussion). Hurley and Lambert[12] commented on this problem in their report on continuous spinal anesthesia with a microcatheter. They suggested that nonuniform distribution of the local anesthetic results from low flow as the local anesthetic leaves the catheter tip owing to the high resistance of the microcatheter. They also suggested that when inadequate anesthesia occurs, the anesthesiologist use a solution of different density and alter the patient's position to "direct" the local anesthetic to the poorly blocked nerves.

Figures 10 to 14, produced with a spinal canal model, suggest a mechanism to account for neural damage after continuous spinal anesthesia.[13] The hypothesis is based on the fact that nerves exposed to large doses of 5% lidocaine may sustain irreversible damage.[19, 23] All of the reported deficits involve the cauda equina. The cauda equina is a group of nerves devoid of protective sheaths that passes through the distal end of the dural sac. Neural toxicity occurs when the cauda equina is exposed to toxic solutions. For example, this happened when large amounts of chloroprocaine (intended for epidural anesthesia) was accidentally injected into the CSF.[9] Normally, 5% lidocaine in 7.5% dextrose is injected as a single dose, and amounts greater than 100 mg are rarely given. However, during continuous spinal anesthesia, more drug can be given when anesthesia is inadequate and 5% lidocaine dosages exceeding 200 mg could cause cauda equina syndrome.

The spinal canal model (Figs. 10–14) is a piece of venous drainage tubing used during open heart surgery, cut to the length of the human dural sac and filled with lactated Ringers solution or 0.9% sodium chloride, both of which have a density similar to CSF. Injections can be made to mimic spinal anesthesia. Local anesthetic solutions are colored with methylene blue dye to aid in viewing the distribution of the local anesthetic. Figure 10 shows the injection of 1 mL of 5% lidocaine in 7.5% dextrose through the Kendall Cospan 28-gauge catheter inserted at the peak of the lumbar lordosis and directed

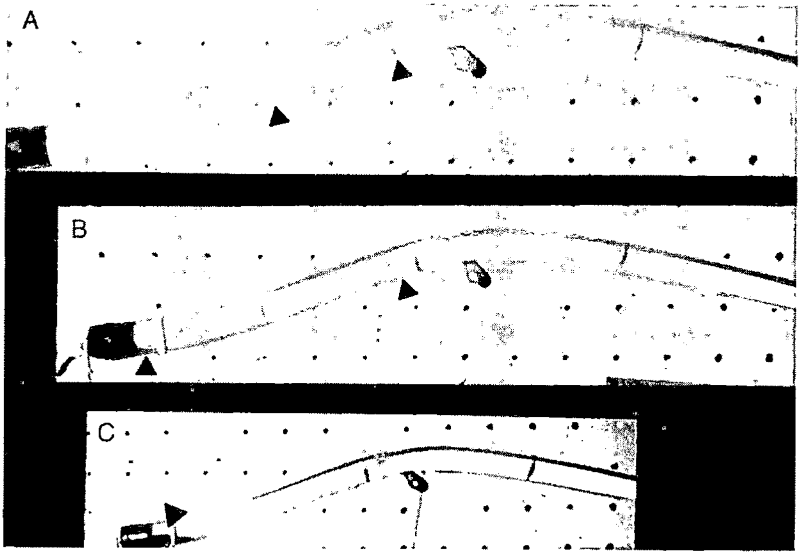

Figure 10. Spinal canal model (see text for details), illustrating the distribution of 1 mL of 5% lidocaine in 7.5% dextrose injected through a 28-gauge catheter. *A*, The stream of lidocaine is only faintly visible (between arrowheads). *B*, The lidocaine rolls along the lower portion of the spinal curve to the sacral end of the model (arrowheads). *C*, The lidocaine pools at the most distal portion of the tube (arrowhead). (*From* Hurley RJ, Lambert DH: Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg 72:817, 1991; with permission.)

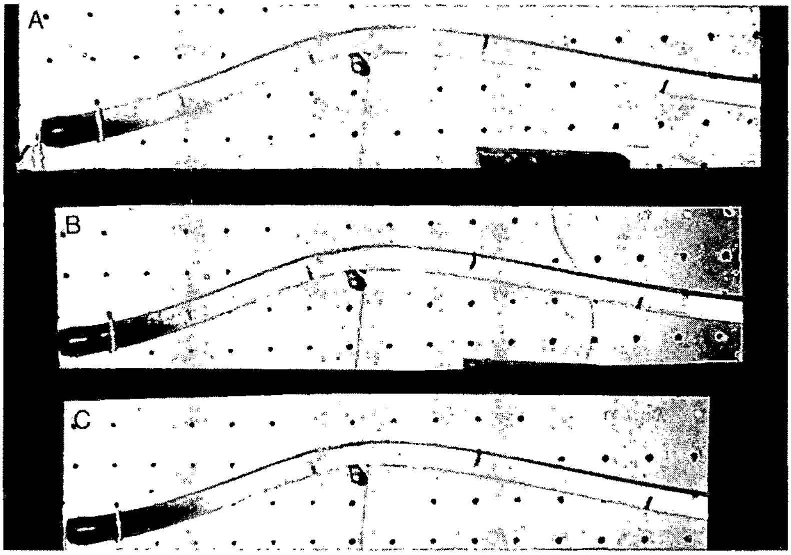

Figure 11. Spinal canal model (see text for details) showing the effect of injecting additional 1-mL volumes of 5% lidocaine in 7.5% dextrose. *A*, Injection of 2 mL of lidocaine (100 mg). *B*, Injection of 3 mL of lidocaine (150 mg). *C*, Injection of 4 mL of lidocaine (200 mg). In the patient, the cauda equina nerves would pass through the pooled lidocaine en route to their destinations. (*From* Hurley RJ, Lambert DH: Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg 72:817, 1991; with permission.)

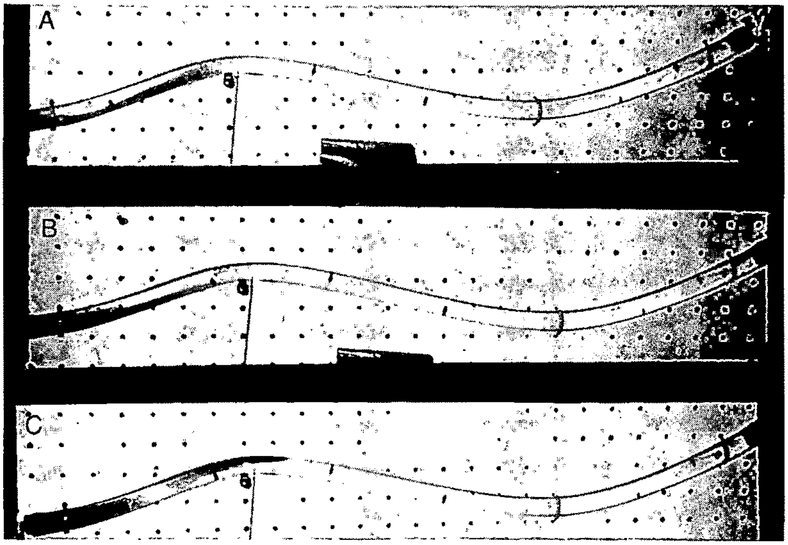

Figure 12. Spinal canal model (see text for details) showing alternative approach to dosing continuous spinal anesthesia when inadequate spinal anesthesia occurs. *A*, Injection of 1 mL of 2% plain lidocaine (20 mg). *B*, Injection of a second mL of 2% lidocaine (40 mg total dose). *C*, Injection of 1 mL of hypobaric 0.375% bupivacaine. (*From* Hurley RJ, Lambert DH: Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg 72:817, 1991; with permission.)

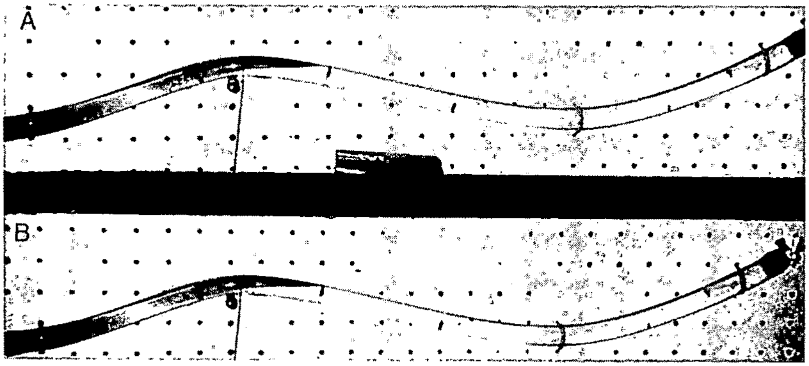

Figure 13. Continuation of Figure 12 showing the effect of injecting an additional 1 mL of hypobaric 0.375% bupivacaine (7.5 mg, total dose). *B* same as *A* but 5 minutes after injection. The spinal canal is nearly uniformly filled with local anesthetic from the peak of the lumbar lordosis and distally. (*From* Hurley RJ, Lambert DH: Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg 72:817, 1991; with permission.)

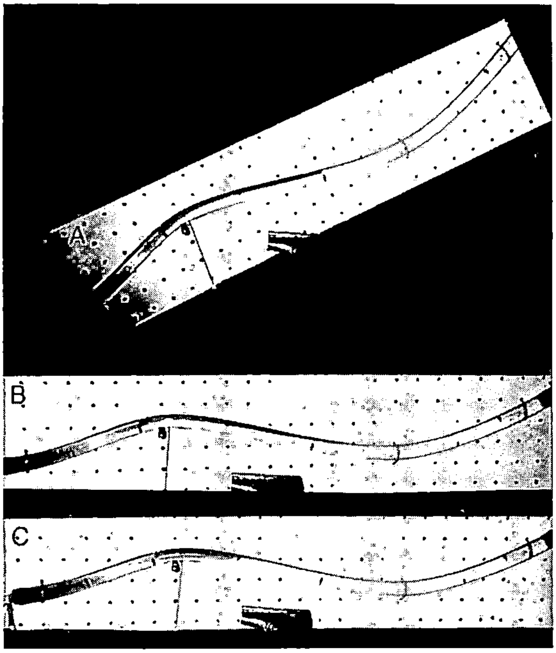

Figure 14. Spinal canal model (see text for details) illustrating the effect of position on the distribution of hypobaric bupivacaine (continuation of Fig. 13). *A*, Head-up posture for 30 seconds. *B*, Returning the model to the supine horizontal position prevents further distribution in the cephalad direction. *C*, With time, the hypobaric bupivacaine migrates back towards the peak of the lumbar lordosis. (*From* Hurley RJ, Lambert DH: Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg 72:817, 1991; with permission.)

caudally a distance of 3 cm (as shown diagrammatically in Fig. 7). The injection was made with a 1-mL tuberculin Luer lock syringe. The stream of local anesthetic is nearly invisible (arrowheads, see Fig. 10*A*). However, it arcs distally, and the local anesthetic, which is very hyperbaric, rolls along the lower portion of the spinal curve (see Fig. 10*B*) to the sacral end of the model. Moments later, the dye is clearly seen as a pooled blue area (see Fig. 10C). Figure 11 shows the effect of injecting an additional 50 mg of 5% lidocaine in 7.5% dextrose (upper panel). The middle and lower panels show the appearance of the dye after injecting a total dose of 150 and 200 mg of lidocaine, respectively. If the 5% lidocaine solution is neurotoxic (and there is evidence that it may be[19, 23]), the cauda equina could be damaged as the nerves pass through the pooled local anesthetic en route to their destinations.

Figure 12 shows an alternative approach for dosing during continuous spinal anesthesia when inadequate anesthesia occurs with 5% lidocaine in 7.5% dextrose. The upper panel shows the injection of 1 mL of 2% plain lidocaine. This solution, reported to be isobaric,[17] is in fact hyperbaric (specific gravity = 1.014, CSF specific gravity = 1.004–1.007, at 20°C), but much less so than 5% lidocaine in 7.5% dextrose (specific gravity > 1.035). The 2% lidocaine solution is distributed more uniformly than the heavier 5% lidocaine in 7.5% dextrose. The middle panel of Fig. 12 shows the injection of an additional 1 mL of 2% lidocaine. At this point, the model contains only 40 mg of lidocaine, but the distribution is equivalent to that which occurs with 150 to 200 mg of 5% lidocaine in 7.5% dextrose. If this does not produce adequate anesthesia, injecting a hypobaric solution, e.g., 0.375% bupivacaine made hypobaric by the addition of an equal volume of distilled water to 0.75% plain bupivacaine, causes wider distribution of anesthetic. This solution is clearly hypobaric (specific gravity = 1.003, 20°C) as shown in Figure 12C. Figure 13*A* shows the injection of an additional milliliter of 0.375% hypobaric bupivacaine. Now, the spinal canal is nearly uniformly filled with local anesthetic from the peak of the lumbar lordosis and distally. Yet, the amounts of local anesthetic are only 40 mg of lidocaine and 7.5 mg of bupivacaine. Should the level of anesthesia at this time be insufficient, repositioning the model for a few seconds as shown in Figure 14*A* directs the hypobaric bupivacaine solution cephalad. Once the solution achieves the desired level, resuming the supine horizontal position prevents further distribution of the hypobaric solution (Fig. 14C, lower panel).

These figures give the anesthesiologist an appreciation for the distribution of local anesthetics within the spinal subarachnoid space when continuous spinal anesthesia is given. Using solutions of lidocaine and bupivacaine in low concentration should prevent cauda equina syndrome.

SUMMARY

Continuous spinal anesthesia has a fascinating history. The recent excitement about being able to use this method in young patients is now dampened by reports of cauda equina syndrome. It is hoped that limiting the concentrations and amounts of local anesthetic used for continuous spinal anesthesia will prevent this. All anesthetic methods have potential for complications and although continuous spinal anesthesia is no exception, it has much to offer.

References

1. Bromage PR: Complications and contraindications. *In* Epidural Analgesia. Philadelphia, Saunders, 1978, p 654
2. Cann JE, Wyscoff CC: Continuous spinal anesthesia: A modification of the ureteral catheter technique. Anesthesiology 9:288, 1948
3. Chen L, Fitzgerald TE, Miller FL, et al: Post dural puncture headache and continuous spinal anesthesia. Reg Anaesth 15:268, 1990
4. Cohen S, Daitch JE, Goldiner PL: An alternative method for management of accidental dural puncture for labor and delivery. Anesthesiology 70:164, 1989
5. Culling RD, Baxter G, Menk EJ: Incidence of postdural puncture headache after continuous spinal anesthesia. Anesthesiology 71:A723, 1989

6. Dean HP: Discussion on the relative value of inhalation and injection methods of inducing anesthesia. Br Med J 5:869, 1907
7. Denny N, Masters R, Pearson D, et al: Postdural puncture headache after continuous spinal anesthesia. Anesth Analg 66:791, 1987
8. Drasner K, Connolly MF, Reece WM: Evaluation of a 28 gauge catheter for continuous spinal anesthesia. Anesth Analg 70:S88, 1990
9. Gissen AJ, Datta S, Lambert DH: The chloroprocaine controversy. II. Is chloroprocaine neurotoxic. Reg Anaesth 9:135, 1984
10. Giuffrida JG, Bizzari DV, Masi R, et al: Continuous procaine spinal anesthesia for cesarean section. Anesth Analg 51:117, 1972
11. Gold BS, Bogetz MS, Orkin F, et al: Continuous spinal anesthesia for ambulatory surgery patients. Anesthesiology 71:A722, 1989
12. Hurley RJ, Lambert DH: Continuous spinal anesthesia with a microcatheter technique: Preliminary experience. Anesth Analg 70:97, 1990
13. Hurley RJ, Lambert DH: Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg, 72:817, 1991
14. Hurley RJ, Lambert DH: Microcatheters for continuous spinal anesthesia [letter]. Anesth Analg 71:201, 1990
15. Hurley RJ: Continuous spinal anesthesia. Int Anesthesiol Clin 27:46, 1989
16. Kallos T, Smith TC: Continuous spinal anesthesia with hypobaric tetracaine for hip surgery in lateral decubitus. Anesth Analg 51:766, 1972
17. Lawrence VS, Rich CR, Magitsky L, et al: Spinal anesthesia with isobaric lidocaine 2% and the effect of phenylephrine. Reg Anaesth 9:17, 1984
18. Lemmon WT: A method for continuous spinal anesthesia. Ann Surg 111:141, 1940
19. Li DF, Bahar M, Cole G, et al: Neurological toxicity of the subarachnoid infusion of bupivacaine, lignocaine or 2-chloroprocaine in the rat. Br J Anaesth 57:424, 1985
20. Lund PC: Continuous spinal techniques. *In* Principles and Practice of Spinal Anesthesia. Springfield, IL, Charles C. Thomas, 1971, p 377
21. Norris MC, Leighton BL: Continuous spinal anesthesia after unintentional dural puncture in parturients. Reg Anaesth 15:285, 1990
22. Peterson DO, Borup JL, Chestnut JS: Continuous spinal anesthesia. Case review and discussions. Reg Anaesth 8:109, 1983
23. Ready LB, Plummer MH, Haschke Rh, et al: Neurotoxicity of intrathecal local anesthetics in rabbits. Anesthesiology 63:364, 1985
24. Reed AP: Microcatheters for continuous spinal anesthesia [letter]. Anesth Analg 71:201, 1990
25. Shroff PK, Skerman JH, Blass NH: Continuous spinal blockade: An old technique revisited. South Med J 81:178, 1988
26. Sutter PA, Gamulin Z, Forster A: Comparison of continuous spinal and continuous epidural anaesthesia for lower limb surgery in elderly patients: A retrospective study. Anaesthesia 44:47, 1989
27. Tuohy EB: Continuous spinal anesthesia: Its usefulness and technique involved. Anesthesia 5:142, 1944
28. Vandam LD, Dripps RD: Long term follow up of patients who received 10,098 spinal anesthetics. III. Syndrome of decreased intracranial pressure (headache and ocular and auditory difficulties). JAMA 161:586, 1956
29. Wissler RN, Bjoraker DG: Continuous spinal anesthesia microcatheters. Anesthesiology Review 17:49, 1990

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NEURAXIAL BLOCKADE FOR CESAREAN DELIVERY

J. Stephen Naulty, MD,
and Richard A. Becker, MD

Cesarean delivery, defined as "delivery of the infant through abdominal and uterine incisions," has over the years progressed from an almost uniformly fatal surgical procedure performed only in emergency situations to a procedure electively performed, with an acceptable complication rate yielding good maternal and neonatal results. The rate of cesarean births has increased from approximately 5% 20 years ago to approximately 25% of births in the United States today. This increased incidence is undoubtedly due to a number of factors, but this increase also attests to the safety of the procedure, particularly (for our purposes) the increased safety and availability of the anesthetic techniques. Anesthesia for cesarean delivery has become extremely reliable and efficacious in achieving the end result of a rapid and safe delivery of the fetus, with minimal maternal morbidity and mortality. Probably the techniques that have produced the majority of this change are neuraxial blocks, i.e., epidural and spinal (subarachnoid) anesthesia. In this review, we describe and examine critically these anesthetic practices and attempt to present a rational method of choosing one of these anesthetic techniques and the appropriate drugs for cesarean delivery.

NEURAXIAL ANESTHETIC TECHNIQUES

Epidural Anesthesia

Perhaps the most noticeable alteration in anesthetic technique for cesarean delivery over the past several decades is the widespread

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adoption of major regional anesthesia, most notably epidural anesthesia. The impetus for this trend stems from alterations in both anesthetic and obstetric practices and teaching. These include an improved understanding of epidural anesthesia in obstetric patients, the introduction of a variety of newer local anesthetic drugs, and the emergence of the anesthesiologist as active participant in obstetric care. As a result, many more anesthesiologists are comfortable with and are well trained in the performance of continuous lumbar epidural anesthesia and analgesia than previously.

Technical Considerations

The various techniques for identification and catheterization of the epidural space are eloquently presented in Bromage's monograph on the subject[20] and are not repeated in detail here. However, several potential advantages of epidural anesthesia over spinal anesthesia are related to specific technical aspects of epidural anesthesia. The first and most important of these advantages is that the insertion of an epidural catheter allows careful titration of anesthetic intensity and extent to precisely that required for the operative procedure. The duration of anesthesia is relatively indefinite and does not require an accurate preoperative prediction of duration. This is particularly important in an era when the duration of cesarean deliveries appears to be on the increase, with much more surgical attention (and consequently, time) paid to hemostatic technique and careful delivery and closure. This alteration in surgical technique is at least in part attributable to modern regional anesthesia, which does not require the "slash and deliver" techniques of the past. In addition, current obstetric practice has resulted in a large number of cesarean deliveries that take place during labor for both fetal and maternal indications. Since many obstetric patients have had continuous epidural anesthetics started for labor analgesia, any subsequent cesarean delivery may be performed using the same anesthetic. In addition to this intraoperative flexibility, continuous epidural anesthesia also allows the popular practice of the use of postoperative epidural opiate analgesia without difficulty.

Several potential disadvantages of epidural anesthesia for cesarean delivery are related to the relative difficulty of the technique. This difficulty is probably most troublesome when one considers the incidence of failure to produce adequate epidural blockade for the procedure, which has been reported to occur in some 2% to 10% of cases.[82]

Many efforts have been made to explain these failures of the technique due to unblocked segments or unilateral blockade on the basis of some subtleties of the anatomy of the epidural space. In addition, anatomic considerations have been used to attempt to explain several observed characteristics of epidural blockade, such as variable density and onset of blockade. Compartmentalization of the epidural space, with subsequent failure of the local anesthetic to reach all the spinal segments required for blockade has been postulated as a reason for these otherwise unexplained failures. The existence of a partial midline septum, the "plica mediana dorsalis" has been described and postulated to be capable of producing this compartmentalization,[15, 69, 115] but its role in influencing the onset of action or spread of epidural anesthesia is in reality only hypothetical.

In our experience, most unilateral blocks or unblocked segments are due to accidental placement of the epidural catheter in the paravertebral space, and most failures of the technique are due to misplacement or accidental removal of the catheter from the epidural space.[12] These misplaced catheters can be repositioned with the subsequent production of satisfactory block in the vast majority of these patients. Some practitioners advocate the injection of a large initial dose (15–25 mL) of local anesthetic through the needle to avoid such failures. However, the use a "single-shot" technique obviates most of the advantages of continuous epidural analgesia, and carries the potential hazard of accidental injection of a large volume of subarachnoid or intravenous local anesthetic, with potentially fatal consequences.

A second reason for failure of epidural anesthesia is inability to produce satisfactory blockade of the sacral nerve roots, most notably S1. A great deal of controversy exists over whether patient position affects subsequent blockade of these sacral nerve roots. Some authors have unequivocally recommended induction of epidural anesthesia in the sitting or semisitting position to allow gravity to encourage the sacral spread of local anesthesia,[7, 8, 9, 30, 31, 128] and others advocate the supine position with left uterine displacement. Most available evidence suggests that gravity minimally affects the epidural spread of local anesthetic.[16, 133] A recent, well-controlled study of the effects of gravity on the onset and extent of sacral anesthesia in parturients undergoing elective cesarean delivery found no difference in the rate of onset or extent of neural blockade between sitting and supine groups.[18] These authors, in a separate study, went on to compare onset and spread of epidural blockade on dependent and nondependent sides during induction of epidural anesthesia for cesarean delivery and again found equal spread of analgesia to pinprick regardless of position.[90] In this study, the lateral supine position was associated with improved acid–base values in umbilical cord blood versus the semisitting supine position, although Apgar and neurobehavioral scores did not differ between the two groups. It appears to us that the adequacy of sacral blockade, the speed of onset, and the extent of neural blockade is not affected by position when relatively large volumes (20–30 mL) of local anesthetic are used. The prime consideration for a position for induction of epidural anesthesia for cesarean delivery should be one that best avoids the maternal supine hypotensive syndrome.

Epidural Venous Cannulation

Placement or movement of the epidural catheter into an epidural vein represents a potentially dangerous and, if unrecognized, sometimes fatal complication. With an incidence ranging from 1% to 10%,[67] it is most likely to occur when the epidural catheter is placed in a position of high epidural venous and azygous flow, i.e., a sitting position where the iliac flow to the inferior vena cava is obstructed and thus rerouted through the azygous system. A recent report indicates that injection of even a small volume of local anesthetic through the epidural needle before introducing the catheter may decrease the incidence of epidural vein cannulation,[9] although this finding has been disputed by Rolbin et al.[112] When using continuous, low-concentration infusions of local anesthetic for labor analgesia, the potential for a toxic level of local anesthetic is extremely low,[83] but in epidural anesthesia for cesarean delivery, where potentially toxic doses of local anesthetic are injected over a shorter period of time, there is great cause for concern.

Several measures have been advocated to minimize or obviate this problem. Careful aspiration through the catheter or lowering the catheter below the level of its entry into the back may reveal an intravenous catheter placement. Test doses of 15 to 20 μg of epinephrine or other β-adrenergic agonists are occasionally useful, although not 100% reliable, to detect an intravenous catheter in the setting of elective cesarean delivery.[6]

Physiologic Considerations

Many practitioners also believe that data exist that suggest that epidural anesthesia has significant physiologic advantages over spinal anesthesia. The impetus for this idea arose to a large extent from data collected in the late 1970s that described favorable overall maternal and neonatal outcomes. In addition, it was suggested that epidural anesthesia was superior to spinal anesthesia because of data suggesting beneficial influences on the ease and safety of the conduct of anesthesia, decreased fetal and neonatal lactic acidosis and higher umbilical blood pH, less frequent and severe maternal hypotension, absence of dural puncture, and perhaps reduced blood loss.[10]

In a physiologic sense, more recent studies have demonstrated that epidural anesthesia is a safe and effective technique for cesarean delivery, but careful attention must be paid to preoperative, intraoperative, and postoperative management of the technique and its complications to realize these potential benefits.

Preoperative Management

High levels of sensory blockade (T2–T4) appear to be necessary for maternal comfort during cesarean delivery. The primary adverse cardiovascular effect of this extensive epidural anesthesia is maternal hypotension secondary to the extensive sympathetic blockade produced by these high thoracic levels of anesthesia. Hypotension is hazardous to both mother and fetus in this setting. Maternal hypotension decreases uterine arterial blood flow and intervillous perfusion and may result in abnormal fetal heart patterns and significant fetal acidosis.[11, 53, 72] The incidence of maternal hypotension secondary to epidural anesthesia for cesarean delivery varies from 5% to 80%.[37, 49, 55, 80] Rapid intravenous infusion of crystalloid solution before inception of the block, left uterine displacement after induction of epidural anesthesia, and prompt correction of maternal hypotension with intravenous ephedrine can minimize maternal hemodynamic and subsequent fetal physiologic changes. The use of prophylactic ephedrine has not proved to be effective in reducing the incidence of hypotension in this setting.[19, 111] Maternal hypotension is more likely in nonlaboring mothers (elective cesarean delivery) than in laboring mothers receiving epidural anesthesia for cesarean delivery. This difference is probably due to the fact that laboring parturients presenting for nonelective cesarean delivery receive, in most hospitals, continuous intravenous hydration only immediately before their regional block. Previously, it has been recommended that 1 L of crystalloid solution be infused before epidural block for elective cesarean delivery. It is likely that this is not a sufficient amount of fluid to prevent hypotension and, in our clinical practice, we routinely infuse 1.5 L of crystalloid solution before induction of elective epidural anesthesia in healthy parturients. We have seen no deleterious effects with the use of this policy and, in fact, several studies support this practice as a means toward preventing maternal hypotension.[25, 80]

Nausea and Vomiting

Prophylactic, preventative measures to reduce nausea and vomiting during cesarean delivery, which are commonly employed before general anesthesia, are more controversial in the case of regional anesthesia. However, any regional technique may involve the loss of protective airway reflexes if complications occur. Because of the parturient's increased risk of pulmonary aspiration of gastric contents, attempts to reduce the gastric volume and acidity as well as the predisposition to vomit seem worthwhile in this population even when performing elective epidural anesthesia.

Choice of Local Anesthetic

If continuous epidural anesthesia is chosen, then a further choice must be made: what local anesthetic should be employed? The ideal local anesthetic is one that reliably produces a dense sensory blockade with minimal uptake into the maternofetal circulation. For successful epidural anesthesia for cesarean delivery, profound sensory blockade is required, to at least the fourth thoracic dermatome. Production of this type of block requires the administration of large doses (20–30 mL) of potent local anesthetics (Table 1). Obviously, these large doses carry the potential for the induction of local anesthetic toxicity, both maternal and fetal. The choice of local anesthetic for any given patient is largely a product of selecting the least toxic drug to achieve the necessary speed of onset and duration of block for the contemplated procedure, with minimal maternal and fetal side effects.

Table 1. USEFUL DRUGS FOR EPIDURAL ANESTHESIA FOR CESAREAN DELIVERY AND POSTPARTUM PROCEDURES

Local Anesthetic	(%)	Onset	Duration (min)	Toxic Plasma Concentration (μg/mL)	Indications	Contraindications
Chloroprocaine	2–3	Rapid	30–45	?	Stat C section	Esterase deficiency
Lidocaine	1.5–2	Rapid	45–60	>5	Elective C section	Fetal distress
Mepivacaine*	1.5–2	Intermediate	60–90	>5	Postpartum operations	Fetal toxicity
Bupivacaine	0.5	Slow	90–120	>1.5 (in pregnancy)	Slow onset C section	Rapid injection
Ropivacaine	0.5	Intermediate	90–120	>4	?	?

*Due to its fetal neurobehavioral effects, mepivacaine is not recommended for cesarean deliveries. Onset and duration times are for purposes of comparison only.

C = cesarean.

Local Anesthetic Toxicity

Because of the slower onset of anesthesia, larger required volume of local anesthetic, and a greater chance of cannulation of epidural veins or failure of the technique, toxic reactions to local anesthetics are of greater concern with epidural than spinal anesthesia. The accidental injection of local anesthetic into an epidural vein delivers a large, direct bolus of drug rapidly to the heart. The severity of this complication is increased in the supine parturient, because the gravid uterus tends to block venous return via the inferior vena cava, creating rapid blood flow through the azygous system and thus both an increased chance of venous puncture and a rapid transport mechanism from the epidural veins to the heart.

The consequences of accidental intravenous injection of local anesthetic have been suggested to be more severe with the use of bupivacaine than with other local anesthetics. Albright[7] became aware of several cases of maternal death attributed to the accidental intravenous injection of a large dose of this concentration of bupivacaine in parturients and published an editorial, "Cardiac Arrest Following Regional Anesthesia with Etidocaine or Bupivacaine." Shortly thereafter, the US Food and Drug Administration banned bupivacaine 0.75% from epidural use in the obstetric population in an attempt to reduce the potential for a large intravascular dose. Since that time, evidence has accumulated that suggests that the potential intrinsic cardiotoxicity of bupivacaine is greater than equipotent doses of lidocaine or 2-chloroprocaine.[76] The susceptibility to cardiotoxic reactions with any local anesthetic appears to be increased in pregnancy. The exact mechanism for this increased sensitivity is unclear but may be due to an increased myocardial delivery or binding of bupivacaine in pregnancy. Alternatively, other authors have postulated an increased sensitivity of the cardiac conducting system to the effects of bupivacaine in pregnancy, perhaps due to the potentiation of local anesthetics by progesterone.[34]

The clinical observation that bupivacaine is more toxic in pregnancy may merely reflect the frequency of bupivacaine usage for obstetric epidural blocks and the higher likelihood of epidural venous puncture with pregnancy, combined with the practical difficulties of performing cardiopulmonary resuscitation on the parturient. It has been recommended that if cardiovascular collapse occurs following intravascular injection of a large dose of local anesthetic, then open chest cardiac massage and immediate delivery may be lifesaving. It is important to realize, however, that the use of lesser concentrations of bupivacaine, 0.5% or 0.25%, does not preclude the possibility of cardiac arrhythmia or arrest secondary to high levels of this drug, and these concentrations may not produce adequate analgesia for cesarean delivery.

Even in the absence of direct intravenous injection, epidural injections of large volumes of local anesthetic can also produce high and potentially toxic serum levels of local anesthetic. A recent study found that the highest plasma bupivacaine levels in parturients undergoing cesarean delivery occurred in patients who received an initial bupivacaine bolus of 20 mL of 0.5% bupivacaine, compared with patients who received a more gradual induction of epidural block.[127] Some of these patients had plasma levels of bupivacaine that have been reported to produce systemic toxicity, although the authors did not observe clinical signs of toxicity in their patients. These investigators noted that peak plasma levels in both groups occurred at the beginning of surgery and during delivery of the infant. The minimum dose of intravenous bupivacaine to have produced cardiovascular collapse in a parturient has been reported to be 25 mg.[7] As a result, we never administer more than 4 mL of 0.5% bupivacaine as a single bolus and administer all local anesthetics as fractionated doses. The adoption of this practice has allowed us to administer more than 20,000 epidural anesthetics in parturients without any clinically evident local anesthetic toxicity. Since, as discussed previously, injection of an initial large bolus provides no significant advantages in terms of speed of onset or incidence of failed blocks, a slow, controlled induction of epidural anesthesia can greatly reduce the risk of local anesthetic toxicity and is an essential element in our practice. If a greater speed of onset is desired, then spinal anesthesia is probably a safer alternative than rapid epidural injections of large doses of local anesthetics.

Fetal and Neonatal Effects of Epidural Anesthesia

Neonatal outcome has been studied closely over the last decade, largely concentrating on the most commonly employed local anesthetics used for this purpose, specifically, mepivacaine 2%, lidocaine 2%, bupivacaine 0.5%, or chloroprocaine 3%.

Bupivacaine. Several studies have used the Brazelton Neonatal Neurobehavioral Assessment Scale[18] to demonstrate what appeared to be significant and consistent long-term neonatal effects of bupivacaine,[81, 114] but were subsequently (in our opinion, correctly) criticized for unrepresentative control groups, inappropriate data analysis, or lack of attention to confounding clinical variables.[62] A recent study of 55 matched mother/infant pairs, using historical controls, found neonatal outcomes as measured by the Brazelton Scale better with bupivacaine than 2-chloroprocaine.[2] In any event, the relatively slow onset and long duration of 0.5% bupivacaine, combined with its potential for severe toxicity, have caused us to only rarely use this drug and only in special circumstances (see following) for continuous epidural anesthesia for cesarean delivery.

Lidocaine. Lidocaine had also been found in early studies to have contributed to lower neonatal neurobehavioral scores when used for epidural analgesia.[50, 118] However, in these studies, lidocaine and mepivacaine were considered together in one group, and more recent work has implicated mepivacaine as the local anesthetic that produced what Scanlon et al[118] referred to as the "floppy-but-alert" neonate in these studies. Numerous recent studies, using a variety of assessment techniques, however, have demonstrated that this phenomenon is not observed when reasonable doses of lidocaine are employed for cesarean delivery.

Abboud et al,[1, 4] in several studies, found no difference in early neonatal neurobehavioral scores (ENNS) of neonates whose mothers received epidural lidocaine for cesarean delivery versus those who received bupivacaine or chloroprocaine; Kuhnert et al[59] used the Brazleton Assessment (undoubtedly the most comprehensive method of neonatal assessment) and found no clinically significant differences in neonates whose mothers received lidocaine or chloroprocaine; and Kileff et al[57] used the Scanlon ENNS to show that infants of mothers receiving 2% lidocaine perform as well as those in the 0.5% bupivacaine group. These data suggest that lidocaine is a safe and efficacious drug when used in judicious amounts for cesarean delivery. Lidocaine 2% with 1/200,000 epinephrine is our usual drug for elective cesarean delivery with epidural anesthesia.

Chloroprocaine. Chloroprocaine, because of its rapid onset, rapid metabolism, and low placental transfer rate,[60] achieved great popularity in obstetrics. It is particularly useful when epidural anesthesia is chosen in cases of fetal distress. Philipson et al[97] found that, even in conditions of fetal acidosis, umbilical vein 2-chloroprocaine levels are similar to those of nonacidotic fetuses.

However, disturbing reports of neurotoxicity occurring after accidental subarachnoid injection of large volumes of 2-chloroprocaine have appeared, which call into question the wisdom of this practice.[77] The usual reason to inject chloroprocaine for cesarean delivery for fetal distress is because of its lack of potential for significant systemic toxicity following rapid injection due to its hydrolysis by serum cholenesterases. However, this practice may be unwise if there is any doubt that the catheter is in the epidural space, because severe neurotoxicity may result from a massive subarachnoid injection. It would appear that this potential for neurotoxicity has to some extent limited the use of this drug.[29, 104, 106]

Investigators have attempted to determine if, in fact, Nesacaine, the commercial preparation of 2-chloroprocaine, is more neurotoxic than other local anesthetics, and whether or not the low pH, the high bisulfite concentration, or the 2-chloroprocaine base are responsible alone or in some combination for these effects. Animal studies have revealed perplexing and mixed results: dog and rabbit data corroborate implications of chloroprocaine neurotoxicity,[103, 129] whereas sheep and monkey data fail to demonstrate intrinsic neurotoxicity of 2-chloroprocaine.[113] Isolated nerve studies have shown that Nesacaine has potential neurotoxicity, with the responsible agent being the combination of sodium bisulfite, 0.2% with a low pH solution; interestingly, even lower concentrations of the bisulfite salt such as that present in commercially prepared bupivacaine and lidocaine, also showed some degree of neurotoxicity.[45] The commercial solution, Nesacaine MPF, has been reformulated with a higher pH and the addition of EDTA as an antioxidant in place of bisulfite. Recently, this formulation has been found to be associated with a high incidence of paralumbar muscle pain following 2-chloroprocaine epidural analgesia in an ambulatory surgical population.[39] There is no evidence suggesting a high incidence of back pain following its use in the obstetric population,[70] but our current practice and recommendation in the care of the parturient is relatively conservative; we reserve 2-chloroprocaine for use in emergency cesarean delivery for fetal distress, where the potential for "acid trapping" of amide local anesthetics in the fetus is considered undesirable. With this approach, we hope to minimize the incidence of neurotoxic complications while at the same time providing an anesthetic with the lowest maternal and fetal risk for a situation of potential fetal hypoxia and acidosis.

Intraoperative Management

Intraoperative maneuvers to avoid or promptly treat cardiovascular compromise during cesarean delivery under epidural anesthesia are essential. Left uterine displacement must be maintained, as maternal supine hypotension secondary to aortocaval compression may cause fetal distress before delivery, maternal nausea and vomiting, and other potentially dangerous and unpleasant sequelae. If maternal hypotension develops, it should be treated immediately with intravenous ephedrine, 5 to 20 mg, repeated as necessary. Recently, Ramanathan and Grant[101] have demonstrated that a low-dose phenylephrine infusion is also a safe and effective treatment for maternal hypotension, if ephedrine is contraindicated. Monitors should include continuous electrocardiographic recordings, automated or manual blood pressure cuff recording measurements every 2 to 3 minutes predelivery and then at 3- to 5-minute intervals until surgery is ended, precordial stethoscope application, pulse oximetry, and some type of temperature probe. Supplemental oxygen via nasal prongs or clear plastic face mask should be administered to increase fetal and maternal Po_2 and oxygen delivery.

Maintenance of Epidural Blockade

Redosing of the epidural catheter is most effective before a detectable decline in anesthetic level occurs; in general, this means 50% to

75% of the original dose of anesthetic administered 10 to 15 minutes before the local anesthetic duration ends. Waiting for the anesthetic level to decline before redosing may confront the anesthesiologist with the unsavory situation of an uncomfortable patient in the middle of surgery due to a relatively abrupt decline in surgical anesthetic level. Again, when redosing the epidural, precautions such as aspiration of the catheter and incremental injection help avoid effects of local anesthetic toxicity. Occasionally, due to either transfer of the patient from the stretcher to the operating table or other patient movement, the epidural catheter becomes dislodged after an initial anesthetic level adequate for the beginning of surgery is established. If attempts to redose the catheter prove unsuccessful during surgery, the temptation is great to provide intravenous or inhalation analgesia to supplement the remaining epidural block. In our opinion, this represents a major hazard to maternal safety during epidural anesthesia for cesarean delivery. Elevated levels of circulating progesterone and β-endorphins sensitize nerve tissue in the parturient to the effects of both inhalation and intravenous anesthetic.[33, 34, 40] In one study minimum alveolar concentration was decreased 25% for halothane, 40% for isoflurane, and 50% for nitrous oxide.[95] Also, the decreased pulmonary function residual capacity and increased alveolar ventilation typical of late pregnancy may result in a more rapid induction of a deeper level of anesthesia with loss of protective airway reflexes.[17] Although inhalational analgesia for labor may entail acceptable risk, we believe that with an ongoing surgical procedure and significant maternal circulating levels of local anesthetic, inhalational or intravenous analgesia during cesarean delivery will greatly increase the risk of silent aspiration of gastric contents, the most common cause of maternal mortality. A recently published analysis of closed insurance claims[21] suggests that excessive sedation during neuraxial anesthesia may also lead to profound hypoxemia and cardiac arrest. Thus, in the event of an inadequate epidural anesthetic with an ongoing cesarean delivery, when no contraindications to general anesthesia exist, we recommend that the epidural technique should be abandoned in favor of a general anesthetic technique with a rapid sequence induction and endotracheal intubation.

Adjuncts to Local Anesthetics

Several classes of drugs have achieved adoption into common practice as adjuncts to increase the speed of onset of local anesthetics, potentiate blockade, or allow decreased doses of local anesthetics in an attempt to minimize both maternal and neonatal effects of local anesthetics. These drugs include catecholamines, narcotics, and alteration of the pH of local anesthetics.

Catecholamines

The addition of epinephrine to local anesthetic solutions, both to increase the depth and duration of epidural blockade and to serve as a potential marker for intravascular placement of epidural catheters, has achieved some popularity in obstetrics. Potentiation of the analgesic effects of local anesthetics by epinephrine is thought to result in part from a local vasoconstrictor effect causing a decrease in absorption of local anesthetic as well as an α-agonist–mediated antinociceptive effect on spinothalamic pathways.[28, 134] While these effects are clearly in evidence with lidocaine, the effects of epinephrine on bupivacaine-produced blockade are less clear. When epinephrine is added to 0.125% or 0.25% bupivacaine for epidural blockade in laboring parturients, the frequency and duration of sensory analgesia are improved,[68] but with concentrations of 0.5% and 0.75% (no longer approved by the Food and Drug Administration for use in obstetrics) studies have revealed both improved[65, 127] and unchanged[107, 122] analgesic efficacy. Some concern exists over the potential effects of α- and β-adrenergic effects of epinephrine on uterine blood flow and uterine contractility. Some investigators have demonstrated decreases in uterine blood flow with the intravenous injection of doses typically employed in epidural anesthesia for cesarean delivery, but others have demonstrated that epinephrine has little effect on placental blood flow in healthy parturients when injected into the epidural space.[78]

Recently, other catecholamine-like drugs, most notably clonidine,[88] have been reported to potentiate local anesthetic blockade.

Alteration of pH

Local anesthetics are weak bases, with the pka typically ranging from 6.5 to 8.0. In aqueous solution, they exist largely in the charged form, and as such, only slowly diffuse into nervous tissue to produce blockade. Hence, the onset of epidural anesthesia ranges from 6 to 25 minutes. In certain situations, such as emergency cesarean delivery, this may be unacceptably long. A great deal of effort has been made to find methods to achieve a more rapid onset of profound epidural anesthesia, with mixed results. One such method has been to increase the fraction of free anesthetic base by altering the pH and composition of the injected local anesthetic solution.

Carbonation of local anesthetics, first reported by Gros in 1910,[47] was one of the first approaches used to achieve this result. In vitro studies by Ritchie et al[108–110] found that an increase in the nonionized fraction of local anesthetic associated with an increase in pH produced both improved nerve penetration and faster onset of neural blockade. Although some reports failed to demonstrate any clinically significant increase in speed of onset with carbonated lidocaine, these studies can be criticized because they failed to measure and report the pH of the local anesthetics used as controls.[71, 79] More recent clinical reports using careful controls have described more extensive and better-quality analgesia attained when using carbonated lidocaine solutions than with lidocaine HCl; the proposed mechanisms include direct depressant effect of carbon dioxide on neural transmission, lower axoplasmal pH resulting in a larger fraction of local anesthetic in the axon itself, and "diffusion trapping" of local anesthetic in the axoplasm secondary to lower intracellular pH.[51] It appears that where carbonated local anesthetics are available (not in the United States) they have established themselves as useful adjuncts for decreasing the latency of epidural anesthesia in the obstetric population.

Recently, the addition of small amounts of sodium bicarbonate to commercially prepared local anesthetic solutions has been reported to produce similar improvements in onset of epidural anesthesia as those achieved with carbonated local anesthetic solutions.[36] One unexpected finding of this research has been to point out the wide variation in pH of commercially prepared local anesthetic solutions and to demonstrate that these differences in pH of the various preparations of local anesthetics may contribute in part to observed differences in the onset and duration found with these drugs. Nesacaine MPF, the most recent commercial formulation of 2-chloroprocaine, shows a more rapid onset with alkalinization,[105, 125] whereas previous Nesacaine solutions did not. It appears that Nesacaine MPF with alkalinization will probably provide the most rapid onset of epidural blockade of currently available local anesthetics.

Carbonation of epidural bupivacaine for cesarean delivery has been less successful. To date, trials of carbonated or alkalinized bupivacaine for cesarean delivery have not shown any dramatic improvement over the hydrochloride salt.[13, 14, 51, 74] Finally, the feasibility of significant pH adjustment of bupivacaine is limited by its rapid precipitation at a pH value greater than 7.0.

Narcotics

In 1979, Wang et al[130] first demonstrated the successful and safe use of intrathecal morphine for patients with chronic pain. Since then various opioids and synthetic opioids have been injected into the epidural space for the production of relief of intraoperative and postoperative pain. Apart from studies of postoperative pain relief with intraspinal opiates for cesarean delivery, very little clinical material exists on the use of epidural narcotics in conjunction with local anesthetic for anesthesia during cesarean delivery, despite their increasing and, in some centers, routine employment for this purpose.

The use of shorter acting, more lipid soluble opiates such as fentanyl and sufentanil combined with local anesthetics have been extensively studied for analgesia for labor and vaginal delivery, and are now being evaluated for anesthesia for cesarean delivery. Several clinical reports using epidural fentanyl in combination with lidocaine or bupivacaine reveal improved maternal comfort levels during the duration of surgery and demonstrate no difference in the condition of the neonates as measured by Apgar scores, neurobehavioral tests, and umbilical cord gases.[43, 75, 99] Plasma fentanyl concentrations obtained from maternal and umbilical cord blood samples are reported to be lower than those observed in studies of epidural fentanyl for labor.[99] Although neonatal blood fentanyl concentrations are below those usually associated with respiratory depression, some investigators have expressed concern regarding the possibility that some neonates might demonstrate extreme sensitivity to respiratory effects of fentanyl,[22, 58] or exhibit excessively high concentrations of the protonated, acid form of fentanyl in the fetal circulation in cases of fetal acidosis,[66] as has been observed with local anesthetics. However, in our opinion, the absence of observed neonatal effects and the low plasma concentrations measured in the most recent studies support the practice of the administration of small (50–100μg), antepartum doses of epidural fentanyl if improved analgesia, particularly the reduction of pain, nausea and vomiting during peritoneal manipulation during cesarean delivery, is desired in nondistressed fetuses.[85] However, this improved analgesia is only observed with lidocaine or bupivacaine, and not with 2-chloroprocaine.[86]

Fentanyl is undoubtedly the drug most commonly employed in the United States for this purpose. Maternal side effects of nausea, vomiting, pruritis, and respiratory depression appear to be minimal owing to the high lipid solubility, with its rapid onset, short duration, and limited effects attributable to rostral spread. Most notably, significant respiratory depression following reasonable doses of fentanyl has not been observed in either healthy volunteers[66] or patients[85] following fentanyl administration. In our current practice we employ epidural fentanyl, 0.7 to 1 μg/kg, for cesarean delivery, which is administered with the initial dose of local anesthetic. We have performed over 20,000 such administrations of epidural fentanyl in the past 8 years without a single case of respiratory depression in the mother or neonate.

Postoperative Complications

Epidural hematoma is a rare but dangerous complication of epidural anesthesia. The population at risk are those parturients with clotting abnormalities or low platelet counts, although a recent report indicates the existence of a small subset of parturients with idiopathically low platelet counts and normal clotting studies.[100] In the case of moderately elevated bleeding times, caution must be observed and risk versus benefit evaluated before establishing any regional anesthetic. The diagnosis of epidural hematoma may be clouded by effects of residual anesthetic blockade, especially in the case of cesarean delivery where higher anesthetic levels of greater density are required: early symptoms, such as worsening low back pain and point tenderness or persistent lower extremity weakness, should not be readily dismissed without ruling out epidural hematoma as the etiologic factor. Early diagnosis (within 6 hours of onset of symptoms) and rapid surgical decompression is the only way to prevent permanent neurologic deficit.

Shivering, a recognized complication of epidural analgesia, may result from several postulated mechanisms, including a direct effect of cold anesthetic solution on thermal receptors within the spinal cord,[98, 126] a differential block of warm and cold afferent thermoreceptor fibers at the dorsal root level,[41] and a drop in core temperature secondary to peripheral vasodilation from sympathetic blockade.[24] While there are no animal data to suggest that differential block or peripheral vasodilation are implicated in shivering, the presence of thermosensitive structures in the spinal cord of various mammalian species is likely.[25, 42] Shivering carries with it the added burden of up to 500% increased oxygen consumption, increased cardiac work, decreased mixed venous oxygen saturation, and increased demand for ventilation, with possible development of hypoxemia and acidosis. The parturient, with the already increased physiologic demands of pregnancy, may face a potentially hazardous situation. In addition, Ostheimer and Datta[94] have noted that shivering alone is the one symptom mentioned by parturients as a particularly disconcerting and unacceptable part of the birth experience. Various treatment modalities have met with mixed results: covering the patient with blankets or warming the operating room seems successful,[96, 120] but warming intravenous fluids or epidural anesthetics has produced variable results.[73, 131, 132] A recent study showed a single dose of intravenous meperidine, 50 mg, after delivery, although producing initial drowsiness, is effective in reducing perioperative shivering during cesarean delivery.[23] Similar responses have been observed following epidural sufentanil administration.[119] The mechanism of this effect remains to be elucidated but may involve modulation of nociceptive and temperature information in the brain and spinal cord.

Dural Puncture

Although avoidance of dural puncture is frequently one of the reasons given to perform epidural rather than spinal anesthesia, accidental dural puncture is the most common complication of epidural anesthesia and results in the syndrome of postdural puncture headache (PDPH), with a frequency as high as 75% when performed with a 17-gauge epidural needle.[92] The incidence of dural puncture depends largely on the experience and skill of the anesthesiologist and in most university training programs is 3% to 5%, with an incidence of probably less than 1% in private practice settings.[91] This headache syndrome, which classically includes frontal or occipital headache worsening with erect posture and, occasionally, tinnitus or photophobia, is usually easy to diagnose, but the differential diagnosis includes migraine, tension or cluster headaches, and even subarachnoid bleed, and these possibilities must be entertained, especially in cases of headache following unrecognized dural puncture.[121] Parturients are probably more susceptible to PDPH because Valsalva maneuvers, dehydration during labor, and postpartum diuresis are likely to reduce the volume of CSF. The direct vasodilatory effects of amide local anesthetics may be a causative agent in the occurrence of PDPH.[87] Cerebral vasodilatation is known to play a role in many types of headaches and, in fact, has been proposed as a mechanism for PDPH, but no conclusive evidence for this mechanism yet exists. Preliminary evidence also suggests that a reduction in incidence of PDPH can be produced with the use of intrathecal fentanyl.[56]

In summary, continuous epidural anesthesia for cesarean delivery is a technique with growing popularity. Its ease of administration in properly trained hands, titratability with respect to density and level of anesthesia, demonstrated maternal safety including retention of protective airway reflexes, minimal fetal and neonatal effects, and allowing the parturient to witness the birth of her child, all serve to substantiate its widespread use for this operative procedure. New local anesthetics and advances in care of premature infants allowing even earlier delivery of compromised fetuses provide areas for much new work using epidural anesthesia in cesarean delivery.

Spinal Anesthesia

Spinal anesthesia at this writing is a commonly used anesthetic for cesarean delivery, and is used for approximately 35% of these procedures nationwide.[44] Reasons for its popularity include speed of induction and onset, the relative simplicity of the technique, minimal fetal and maternal exposure to drugs, and good predictability and reliability. As with epidural anesthesia, the parturient remains awake and alert, minimizing the risk of aspiration. Much work over the last decade has attempted to idealize a drug combination for subarachnoid block in cesarean delivery while reducing the disadvantages of a more profound hypotension, intrapartum nausea and vomiting, and potential PDPH.

Technical Considerations

The primary advantage of spinal anesthesia over epidural anesthesia for cesarean delivery is its relative ease of administration. The technique for single-shot spinal anesthesia is well described and well understood by nearly all anesthesiologists. One of the primary advantages of spinal anesthesia for cesarean delivery is the use of much smaller amounts of local anesthetic to produce surgical anesthesia than that employed with epidural anesthesia, thus minimizing maternal and neonatal effects of the drug. Dose requirements for spinal anesthesia are reduced 30% to 50% in the pregnant patient (compared with the nonpregnant state), probably due to a combination of decreased volume of the epidural and subarachnoid spaces secondary to epidural venous congestion, and biochemical and hormonal changes that may alter neuronal responsiveness to local anesthetics.[34] These reduced doses, at least with lidocaine[63] or bupivacaine,[64] are associated with lower maternal and neonatal blood levels of local anesthetic than those obtained with epidural anesthesia.[61] While neurobehavioral evaluation of the neonates in these studies was not performed, previous studies have demonstrated no known neurobehavioral effects from even larger concentrations of bupivacaine or lidocaine in patients receiving epidural anesthesia. Compared with general anesthesia, spinal anesthesia is associated with higher scores on the Early Neurobehavioral Scale and Neonatal Neurologic and Adaptive Capacity Scores.[3, 52]

Most spinal anesthetics are performed as a single-shot technique, and, therefore, it is extremely important to provide an adequate, evenly distributed anesthetic from the outset, as the addition of more local anesthetic to supplement the block, as can be done with continuous techniques, is not possible. Sprague[124] experimented with right and left side lateral decubitus positions followed by uterine displacement with or without a 12-cm right hip wedge and found that only in the right side down position followed by right hip wedge was adequate anesthesia for the duration of cesarean delivery consistently produced. Induction with the left side down followed by a right hip wedge resulted in sensory level that was four to five dermatomes lower than that on the left and resulted in a higher percentage of patients who required supplemental general anesthesia.

In the event of either minimal or no detectable sensory/motor blockade after induction of spinal anesthesia but before incision, the technique should be repeated, if time permits. The dosage of local anesthetic should be decreased by the fraction of the dermatomes that are already blocked. For example, if an initial dose of local anesthetic results in a block to T12, then 10 of the needed 20 dermatomes are already blocked. A supplemental injection of half the initial dose should be administered to achieve adequate sensory analgesia for the operation. Discovery of an inadequate spinal block after the beginning of surgery, however, must result in a rapid sequence induction of general anesthesia in order to maintain the highest degree of maternal and neonatal safety. High doses of supplemental intravenous analgesics or sedatives should be avoided, as unrecognized hypoxia or aspiration may occur, with disastrous consequences.

Physiologic Considerations

On the other hand, it is difficult to attribute any particular physiologic advantages of spinal anesthesia over epidural anesthesia. The incidence of maternal hypotension is much higher and more profound than following epidural block; in one study as high as 80%.[27] These hemodynamic changes result from the rapid onset of direct blockade of sympathetic vasomotor activity and are compounded by compression of the inferior vena cava by the gravid uterus when the patient is supine. Maternal hypotension is a more frequent occurrence in nonlaboring women undergoing subarachnoid block for elective cesarean delivery, probably due to a less adequate hydrational status than parturients previously in labor with a continuous intravenous infusion of a balanced salt solution. Several maneuvers are useful to prevent maternal hypotension after spinal blockade: infusion of 2 L of balanced salt solution before induction, left uterine displacement throughout induction and cesarean delivery, and prompt treatment with supplemental intravenous fluid boluses and intravenously administered ephedrine (5–20 mg) will reestablish normotension, reduce the incidence of maternal nausea and vomiting, and improve neonatal acid–base status. The prophylactic administration of ephedrine is a controversial practice. An intramuscular dose of 50 mg of ephedrine before induction of subarachnoid block will indeed reduce the incidence of maternal hypotension,[48] but it is debatable whether the approximately 50% of parturients who remain normotensive without vasopressors should receive ephedrine. There is no evidence to show that prophylactic treatment of hypotension with vasopressors is better than prompt treatment, with respect to maternal and neonatal outcome.

Nausea and vomiting are common complications of spinal anesthesia and have been attributed to psychogenic factors as well as uncorrected hypotension with decreased cerebral blood flow, visceral traction, narcotic supplementation, and inadequate sensory level.[32, 102] In our experience, the most common cause of intraoperative nausea is hypotension. The best treatment for nausea and vomiting secondary to hypotension is restoration of normal blood pressure with a vasopressor such as ephedrine that preserves uterine blood flow. In the absence of hypotension, a small dose (0.625–1.25 mg) of droperidol is effective as prophylaxis or treatment of maternal nausea and vomiting during spinal anesthesia for cesarean delivery, with no adverse neonatal effects.[38, 116] Metoclopromide also may be effective as an antiemetic in this situation.

Respiratory and subsequent cardiac arrest secondary to high cervical block, the so-called "total spinal," can occur rapidly and requires prompt recognition and management to prevent adverse sequelae to mother and infant. Treatment consists of establishing an airway and ventilating with cricoid pressure and 100% oxygen. Although the anesthesiologist may be tempted to "decrease the level" of anesthesia by using the *reverse* Trendelenburg (head up) position, such a maneuver will only worsen an already severe hypotension, with little effect on the level of spinal anesthesia. Thus, restoring blood pressure with fluids, vasopressors, and the Trendelenburg position (head down) are essential after the airway is established. While succinylcholine, 1 to 1.5 mg/kg, may be administered intravenously to facilitate endotracheal intubation, it is seldom required, and the use of small doses of induction agents such as thiopental, midazolam, or even etomidate to provide amnesia may lead to cardiovascular collapse.

Some of these difficulties attributable to the single-shot nature of contemporary spinal anesthesia may be obviated with continuous spinal anesthesia. Continuous spinal anesthesia was first reported in 1907 when the British surgeon Dean placed a needle in the subarachnoid space and left it in situ, intermittently dosing the patient through the needle,[35] and was frequently used in the 1940s and 1950s; it subsequently lost its popularity with the advent of continuous epidural anesthesia, which possessed a lower incidence of PDPHs. The most recent series of continuous spinal anesthesia for cesarean delivery used 24-gauge catheters through 21-gauge needles and reported an incidence of PDPH near 16%, not an unexpected number with a 21-gauge puncture and inattention to bevel direction, as seen in this study.[46] Recent technologic and material advances have provided us with much smaller-gauge spinal needles and catheters (26–32 gauge). In our experience, the incidence of PDPH with these small needles and catheters is comparable with that actually produced in practice with continuous lumbar epidural analgesia (1.6% versus 2%, respectively).[84] If the incidence of PDPH is indeed acceptably low, we expect this objection to the technique to become invalid.

The efficacy of conduction anesthesia in cesarean delivery has been reported to be more satisfactory with spinal than with epidural anesthesia (92% versus 82% in one study).[93] Therefore, compared with epidural anesthesia, continuous spinal anesthesia possesses the advantages over epidural anesthesia of a more rapid onset, a higher degree of reliability with little requirement for technical expertise, and a lower dose of local anesthetic. In short, this technique offers the advantages offered by single-shot spinal anesthesia, with the addition of a controllable duration, intensity, and level of anesthesia, making this technique ideal for elective as well as urgent cesarean delivery. It is also conceivable that continuous spinal anesthesia possesses a decreased potential for airway, cardiovascular, and respiratory complications and a greatly diminished possibility of local anesthetic toxicity as compared with general or epidural anesthesia, although more widespread use will be necessary to support the validity of these assumptions.

Choice of Local Anesthetic

The choice of local anesthetics for spinal anesthesia in cesarean delivery is based primarily on the desired duration of action (Table 2). The short duration of lidocaine necessitates completion of surgery within 45 minutes; prolongation of the block with epinephrine is controversial and probably clinically nonsignificant.[78, 123] Hyperbaric bupivacaine, 0.75% and 0.5%, has been shown to provide safe and effective anesthesia for cesarean delivery, although 0.5% bupivacaine is not available for general use in the United States.[117] The use of bupivacaine for spinal anesthesia for cesarean delivery appears to produce less motor block than subarachnoid lidocaine, tetracaine, and etidocaine. Because profound motor blockade is not necessary for this operation, the decreased maternal anxiety observed with decreased motor block may be an advantage.[26] The addition of 0.2 mg of epineph-

Table 2. USEFUL DRUGS FOR SPINAL ANESTHESIA FOR CESAREAN DELIVERY*

Local Anesthetic	Concentration	Dose	Onset	Duration (min)	Duration with .2 mg EPI
Lidocaine-glucose	5% Lidocaine/ 7.5% glucose	75 mg (1.5 mL)	Rapid	45–60	60–75
Bupivacaine-glucose	0.75% Bupivacaine/ 8.25% glucose	11.2–15 mg (1.5-2 mL)	Intermediate	60–90	70–110
Tetracaine-glucose	0.5% Tetracaine/ 5% glucose	7.5–10 mg (1.5–2 mL)	Slow	90–120	120–150
Tetracaine-procaine	0.5% Tetracaine/ 10% procaine	7.5 mg Tetracaine/ 75 mg procaine	Rapid	90–120	120–150

*Onset and duration times are for purposes of comparison only.
Abbreviation: EPI = epinephrine.

rine to 0.75% hyperbaric bupivacaine improves the quality of analgesia and increases the duration of sensory and motor anesthesia.[59] A recent study indicates that addition of the lipid soluble narcotic fentanyl in doses as small as 6.25 μg to hyperbaric bupivacaine spinal significantly improves intraoperative analgesia, with no adverse effects on mother or neonate.[54] Because of its less predictable onset of action and duration and an occasionally unsatisfactory degree of sensory blockade, the use of hyperbaric 1% tetracaine is declining for cesarean delivery. The addition of epinephrine does not appear to potentiate sensory block with this drug as it does with bupivacaine, but does significantly increase the duration of motor block, and hence recovery time. If the long durations of spinal anesthesia produced by tetracaine are required, the substitution of 10% procaine for 10% glucose as the hyperbaric diluent seems to provide a rapid, reliable onset of sensory block. This hyperbaric solution, compared with an equal dose of tetracaine with dextrose, provides better sensory anesthesia without any differences in the duration of motor or sensory block, incidence of hypotension, neonatal Apgar scores, or umbilical cord blood gases.[26]

SUMMARY

Neuraxial blockade (spinal and epidural anesthesia) has become the primary means of administering anesthesia for cesarean delivery in the United States. These techniques, when properly administered, allow the production of nearly ideal operating conditions, excellent maintenance of both maternal and fetal homeostasis, and offer the advantages of an awake, cooperative, and participating patient during the birth process. These advantages over general anesthesia are considerable, and with proper attention to the details of management, as elucidated previously, safe and effective anesthesia can be provided with these techniques. However, the apparent safety of these techniques require even more vigilance by the anesthesiologist to detect as early as possible the occasionally disastrous complications that may arise, and the practitioner of these techniques must be ready to treat at any time the oftentimes unbelievably rapid development of life-threatening complications.

References

1. Abboud TK, Khoo SS, Miller F, et al: Maternal, fetal, and neonatal responses after epidural analgesia with bupivacaine, 2-chlorprocaine, or lidocaine. Anesth Analg 61:638–644, 1982
2. Abboud TK, Kim KC, Noviehed R, et al: Epidural bupivacaine, chlorprocaine, or lidocaine for cesarean section—Maternal and neonatal effects. Anesth Analg 62:914–919, 1983
3. Abboud TK, Nagappala S, Murakauak, et al: Comparison of the effects of general and regional anesthesia for cesarean section on neonatal neurologic and adaptive capacity scores. Anesth Analg 69:996–1000, 1985
4. Abboud TK, Sarkis F, Blikian G, et al: Lack of adverse neurobehavioral effects of lidocaine. Anesthesiology 57:A404, 1982
5. Abouleish EI: Epinephrine improves the quality of spinal hyperbaric bupivacaine for cesarean section. Anesth Analg 66:395–400, 1987
6. Abraham RA, Harris AP, Maxwell LG, et al: The efficacy of 1.5% lidocaine with 7.5% dextrose and epinephrine as an epidural test dose for obstetrics. Anesthesiology 64:116–119, 1986
7. Albright GA: Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. Anesthesiology 51:285–287, 1979
8. Albright GA, Joupilla R, Hollmen A, et al: Epinephrine does not alter human intervillous blood flow during epidural anesthesia. Anesthesiology 54:131–135, 1981
9. Alin NW, Ung DA, DeFay S, et al: Blood vessel puncture with epidural catheters. Anesthesiology 71:A916, 1989
10. Ansbro FP, Gordon CA, Bodell BB, et al: Epidural anesthesia for cesarean section. Report of 125 cases. NY State J Med 32:1901–1905, 1952
11. Antoine C, Young BK: Fetal lactic acidosis with epidural anesthesia. Am J Obstet Gynecol 142:55–59, 1982
12. Asato F, Hirakawa N, Oda M, et al: A median epidural septum is not a common cause of unilateral epidural blockade. Anesth Analg 71:427–429, 1990
13. Bedder MD: Comparison of bupivacaine and alkalinized bupivacaine in brachial plexus anesthesia. Anesth Analg 67:48–52, 1988
14. Benhamou D, et al: Alkalinization of epidural 0.5% bupivacaine for cesarean section. Reg Anesth 14:240–243, 1989
15. Blomberg R: The dorsomedian connective tissue band in the lumbar epidural space of humans: An anatomical study using epiduroscopy in autopsy cases. Anesth Analg 65:47–52, 1986
16. Bonica JJ: Obstetric Anesthesia and Analgesia. Amsterdam, World Federation of Anesthesiologists, 1980
17. Bonica JJ: Physiology of pregnancy. *In* Principles and Practice of Obstetric Analgesia and Anesthesia. Philadelphia, Davis, 1972, pp 21–26
18. Brazelton TB: Neonatal Behavioral Assessment Scale, ed 2. Philadelphia, Lippincott, 1984
19. Brizgys RV, Dailey PA, Shnider SM, et al: The incidence and neonatal effects of maternal hypotension during epidural anesthesia for cesarean section. Anesthesiology 67:782–786, 1987

20. Bromage PR: Epidural Analgesia. Philadelphia, Saunders, 1978
21. Caplan RA, Ward RJ, Posner K, et al: Unexpected cardiac arrest during spinal anesthesia: A closed claims analysis of predisposing factors. Anesthesiology 68:5–11, 1988
22. Carrie LES, O'Sullivan GM, Seegobin R: Epidural fentanyl in labor. Anaesthesia 36:965–969, 1981
23. Casey WF, Smith CE, Katz JM, et al: Intravenous meperidine for control of shivering during caesarean section under epidural anaesthesia. Can J Anaesth 35:128–133, 1988
24. Chamberlain DP, Chamberlain DDL: Changes in the skin temperature of the trunk and their relationship to sympathetic blockade during spinal anesthesia. Anesthesiology 65:139–143, 1986
25. Chambers WW, Seigel MS, Liu JC, et al: Thermoregulatory responses of decerebrate and spinal cats. Exp Neurol 42:282–299, 1974
26. Chantigian RC, Datta S, Burger GA, et al: Anesthesia for cesarean delivery utilizing spinal anesthesia. Tetracaine versus tetracaine and procaine. Reg Anesth 9:195–199, 1984
27. Clark RB, Thompson DS, Thompson CH: Prevention of spinal hypotension associated with cesarean section. Anesthesiology 45:670–674, 1976
28. Collins JG, Kitahata LM, Matsumoto M, et al: Spinally administered epinephrine suppresses noxiously evoked acitivity of WDR neurons in the dorsal horn of the spinal cord. Anesthesiology 60:269–275, 1984
29. Covino BG, Marx GF, Finster M: Prolonged sensory/motor deficits following inadvertent spinal anesthesia. Anesth Analg 59:399–400, 1980
30. Crawford JS: Experiences with lumbar extradural analgesia for Caesarean section. Br J Anaesth 52:821, 1980
31. Datta S, Alper MH, Ostheimer GW, et al: Effects of maternal position on epidural anesthesia for Cesarean section: Acid-base status and bupivacaine concentrations at delivery. Anesthesiology 50:9, 1979
32. Datta S, Alper MH, Ostheimer GW, et al: Method of ephedrine administration and nausea and hypotension during spinal anesthesia for cesarean section. Anesthesiology 56:68–73, 1982
33. Datta S, Hurley RJ, Naulty JS, et al: Plasma and cerebrospinal fluid progesterone concentrations in pregnant and non-pregnant women. Anesth Analg 65:950–954, 1986
34. Datta S, Lambert DH, Gregus J, et al: Differential sensitivities of mammalian nerve fibers during pregnancy. Anesth Analg 62:1070–1072, 1983
35. Dean HP: Discussion on the relative value of inhalation and injection methods of inducing anesthesia. Br Med J 5:869–877, 1907
36. Difazio CA, Carron H, Grosslight KR, et al: Comparison of pH-adjusted lidocaine solutions for epidural anesthesia. Anesth Analg 65:760–764, 1986
37. Downing JW, Houlton PC, Barclay A: Extradural analgesia for cesarean section: A comparison with general anesthesia. Br J Anaesth 51:367–374, 1979
38. Edelman C, Karambelkar D, Kennedy R, et al: Neonatal effects after maternal prophylactic use of droperidol. *In* Abstracts of Scientific Papers, Annual Meeting of the Society for Obstetric Anesthesia and Perinatology, Washington, DC, 1985, p 48
39. Fibuch EE, Opper SE: Back pain following epidurally administered nesacaine-MPF. Anesth Analg 69:113–115, 1989
40. Flanagan HL, Datta S, Lambert DH, et al: Effect of pregnancy on bupivacaine-induced conduction blockade in the isolated rabbit vagus nerve. Anesth Analg 66:123–126, 1987
41. Fruhstorfer H, Zenz M, Nolte H, et al: Dissociated loss of cold and warm sensibility during regional anesthesia. Pflugers Arch 349:73–82, 1974
42. Fuller CA, Horowitz JM, Horwitz BA: Spinal cord thermosensitivity and sorting of neural signals in cold exposed rats. J Appl Physiol 42:154–158, 1977
43. Gaffud MP, Bansal P, Lawton C, et al: Surgical analgesia for cesarean delivery with epidural bupivacaine and fentanyl. Anesthesiology 65:331–334, 1986
44. Gibbs CP, Krischer J, Peckham BM, et al: Obstetric anesthesia: A national survey. Anesthesiology 65:298–306, 1986
45. Gissen AJ, Datta S, Lambert D: The chlorprocaine controversy. II. Is chlorprocaine neurotoxic? Reg Anesth 9:135–145, 1984

46. Giuffrida JG, Bizzarri DV, Masi R, et al: Continuous procaine spinal anesthesia for cesarean section. Anesth Analg 51:72–74, 1972
47. Gros O: Uber die narkotica und lokalanasthetica. Arch Exp Pathol Pharmakol 63:80–106, 1910
48. Gutsche BB: Prophylactic ephedrine preceding spinal analgesia for cesarean section. Anesthesiology 45:462–465, 1976
49. Hallworth D, Jellicoe JA, Wilkes RG: Hypotension during epidural anesthesia for cesarean section. A comparison of intravenous loading with crystalloid and colloid solutions. Anaesthesia 38:250–253, 1983
50. Higuchi M, Takeuchi S: Studies on the neurobehavioral response (Scanlon test) in newborns after epidural anesthesia with various anesthetic agents for cesarean section. Acta Obstet Gynecol Jpn 4:2143–2148, 1982
51. Hilgier M: Alkalinization of bupivacaine for brachial plexus block. Reg Anesth 10:59–61, 1985
52. Hodgkinson R, Bahtt M, Kim SS, et al: Neonatal neurobehavioral tests following cesarean section under general and spinal anesthesia. Am J Obstet Gynecol 132:670–674, 1978
53. Hon EH, Reid BL, Hehre FW: The electronic evaluation of fetal heart rate. II. Changes with maternal hypotension. Am J Obstet Gynecol 79:209–215, 1960
54. Hunt CO, Naulty JS, Bader AM, et al: Perioperative analgesia with subarachnoid fentanyl—Bupivacaine for cesarean delivery. Anesthesiology 71:535–540, 1989
55. James FM III, Crawford JS, et al: A comparison of general anesthesia and lumbar epidural analgesia for elective cesarean section. Anesth Analg 56:228–235, 1977
56. Johnson MD, Hertwig L, Vehring PH, et al: Intrathecal fentanyl may reduce the incidence of spinal headache. Anesthesiology 71:A911, 1989
57. Kileff ME, James FM III, Dewan DM, et al: Neonatal neurobehavioral responses after epidural anesthesia for cesarean section using lidocaine and bupivacaine. Anesth Analg 63:413, 1984
58. Koehntep DE, Rodman JH, Brundage DM, et al: Pharmacokinetics of fentanyl in neonates. Anesth Analg 65:227–232, 1986
59. Kuhnert BR, Harrison MJ, Linn PL, et al: Effect of maternal epidural anesthesia on neonatal behavior. Anesth Analg 63:301–308, 1984
60. Kuhnert BR, Kuhnert PM, Prechouska AL, et al: Plasma levels of 2-chlorprocaine in obstetrical patients and their neonates after epidural anesthesia. Anesthesiology 53:21, 1980
61. Kuhnert PM, Kuhnert BR, Stitts JM, et al: The use of a selected ion monitoring technique to study the disposition of bupivacaine in mother, fetus, and neonate following epidural anesthesia for cesarean section. Anesthesiology 55:611–617, 1981
62. Kuhnert BR, Linn PL, Kuhnert PM: Obstetric medication and neonatal behavior—Current controversies. Clin Perinatol 12:23–39, 1985
63. Kuhnert BR, Philipson EH, Pimental R, et al: Lidocaine disposition in mother, fetus, and neonatal after spinal anesthesia. Anesth Analg 65:139–144, 1986
64. Kuhnert BR, Zuspank J, Kuhnert P, et al: Bupivacaine disposition in mother, fetus, and neonate after spinal anesthesia. Anesth Analg 66:407–412, 1986
65. Laishley RS, Morgan BM, Reynolds F: Effect of adrenaline on extradural anaesthesia and plasma bupivacaine concentrations during caesarean section. Br J Anaesth 60:180–186, 1988
66. Lam AM, Knill RL, Thompson WR, et al: Epidural fentanyl does not cause delayed respiratory depression. Can Anaesth Soc J 30:578–579, 1983
67. Leighton BL, Norris MC, DeSimone CA, et al: The air test as a clinically useful indicator of intravenously placed epidural catheters. Anesthesiology 73:610–613, 1990
68. Littlewood DG, Buckley P, Covino BG, et al: Comparative study of various local solutions in epidural block in labour. Br J Anaesth 51:47S, 1979
69. Luyendijk W: The plica mediana dorsalis of the dura mater and its relation to lumbar peridurography (canalography). Neuroradiology 11:147–149, 1976
70. MacArthur C, Lewis M, Knox EG, et al: Epidural anaesthesia and long term backache after childbirth. Br Med J 301:9–12, 1990
71. Martin R, Lamarche Y, Tetreault L: Comparison of the clinical effectiveness of

lidocaine hydrocarbonate and lidocaine HCl with and without epinephrine in epidural anaesthesia. Can Anaesth Soc J 28:217–223, 1981

72. Marx GF, Cosmi EV, Wollman SB: Biochemical status and clinical condition of mother and infant at cesarean section. Anesth Analg 48:986–994, 1969
73. McCarroll SM, Cartwright P, Weeks SK, et al: Warming intravenous fluids and the incidence of shivering during caesarean section under epidural anaesthesia. Can J Anaesth 33:S72–S73, 1986
74. McMarland GH, et al: Effect of pH adjustment of bupivacaine on onset and duration of epidural analgesia in parturients. Can Anaesth Soc J 33:537–541, 1986
75. Milon D, Bentue-Ferrer D, Noury D, et al: [Epidural anesthesia using the bupivacaine-fentanyl combination for cesarean section]. Anesthesia peridurale pour cesarienne par association bupivacaine-fentamyl. Ann Fr Anesth Reanim 2:273–279, 1983
76. Moller R, Covino BG: Cardiac electrophysiologic properties of bupivacaine and lidocaine compared with those of ropivacaine, a new amide local anesthetic. Anesthesiology 72:322–329, 1990
77. Moore DC, Spierdijk J, vanKleef JD, et al: Chlorprocaine neurotoxicity: Four additional cases. Anesth Analg 61:155–159, 1982
78. Moore DS, Chadwick HS, Ready LB: Epinephrine prolongs lidocaine spinal: Pain in the operative site the most accurate method of determining local anesthetic duration. Anesthesiology 67:416–418, 1987
79. Morison DH: A double-blind comparison of carbonated lidocaine and lidocaine HCl in epidural anesthesia. Can Anaesth Soc J 28:387–389, 1981
80. Murray AM, Morgan M, Whitman JG: Crystalloid versus colloid for circulatory preload for epidural cesarean section. Anaesthesia 44:463–466, 1989
81. Murray AD, Dolby RM, Nation RL, et al: Effects of epidural anesthesia on newborns and their mothers. Child Dev 52:71–82, 1981
82. Narang VP, Linter SP: Failure of extradural blockade in obstetrics. A new hypothesis. Br J Anaesth 60:402–404, 1988
83. Naulty JS: Continuous infusions of local anesthetics and narcotics for epidural analgesia in the management of labor. Int Anesth Clin 28:17–18, 1990
84. Naulty JS, Barnes D, Becker RB, et al: Continuous subarachnoid sufentanil for labor analgesia. Anesthesiology 73:A 964, 1990
85. Naulty JS, Datta S, Ostheimer GW, et al: Epidural fentanyl for post caesarean delivery pain management. Anesthesiology 63:694–698, 1985
86. Naulty JS, Hertwig L, Hunt CO, et al: Duration of analgesia of epidural fentanyl following cesarean delivery—Effects of local anesthetic drug selection. Anesthesiology 65:A180, 1986
87. Naulty JS, Hertwig L, Hunt CO, et al: Influence of local anesthetic solution on post dural puncture headache. Anesthesiology 72:450–455, 1990
88. Nishikawa T, Dohi S: Clinical evaluation of clonidine added to lidocaine solution for epidural anesthesia. Anesthesiology 73:853–859, 1990
89. Norris MC, Dewan DM: Effect of gravity on the spread of extradural anaesthesia for caesarean section. Br J Anaesth 59:338–341, 1987
90. Norris MC, Leighton BL, De Simone CA, et al: Lateral position and epidural anesthesia for cesarean section. Anesth Analg 67:788–790, 1988
91. Ong B, Cohen MM, Cumming M, et al: Obstetrical anaesthesia at Winnipeg Women's Hospital 1975–83: Anaesthetic techniques and complications. Can J Anaesth 34:294–299, 19XX
92. Ostheimer GW: Headache in the postpartum period. *In* Marx GF (ed): Clinical Management of Mother and Newborn. New York, Springer-Verlag, 1979, pp 27–41
93. Ostheimer GW: The labor and delivery suite. *In* Ostheimer GW (ed): Manual of Obstetric Anesthesia. New York, Churchill Livingstone, 1984, pp 399–412
94. Ostheimer GW, Datta S: Observations in the post partum recovery room after various local anesthetic techniques. Reg Anesth 6:13–17, 1981
95. Palahnick RJ, Shnider SM, Eger EI II: Pregnancy decreases the requirement for inhaled anesthetic agents Anesthesiology 41:82–83, 1974
96. Pflug AE, Aasheim GM, Foster C, et al: Prevention of post anesthesia shivering. Can Anaesth Soc J 25:43–49, 1978
97. Philipson EH, Kuhnert BR, Syracuse CD: Fetal acidosis, 2-chlorprocaine, and epidural anesthesia for cesarean section. Am J Obstet Gynecol 151:322–324, 1984

98. Ponte J, Collett BJ, Walmsley A: Anesthetic temperature and shivering in epidural anaesthesia. Acta Anaesthesiol Scand 30:584–587, 1986
99. Preston PG, Rosen MA, Hughes SC, et al: Epidural anesthesia with fentanyl and lidocaine for cesarean section: Maternal effects and neonatal outcome. Anesthesiology 68:938–942, 1988
100. Ramanathan J, Sibai BM, Vu T, et al: Correlation between bleeding times and platelet counts in women with preeclampsia undergoing cesarean section. Anesthesiology 71:188–191, 1989
101. Ramanathan S, Grant GJ: Vasopressor therapy for hypotension due to epidural anesthesia for cesarean section. Acta Anaesthesiol Scand 32:559–565, 1988
102. Ratra CK, Badola RP, Bhargava KP: A study of factors concerned in emesis during spinal anaesthesia. Br J Anaesth 44:1208–1211, 1972
103. Ravindran RS, Turner MS, Muller J: Neurologic effects of administration of 2-chlorprocaine-CE, bupivacaine, and low pH normal saline in dogs. Anesth Analg 61:279–283, 1982
104. Ravindran RS, Bond VK, Tasch M, et al: Prolonged neural blockade following regional analgesia with 2-chlorprocaine. Anesth Analg 59:447–451, 1980
105. Redick LF: pH adjustment of 2-chlorprocaine solutions. Anesth Analg 66:283–286, 1987
106. Reisner LS, Hochman BN, Plumer M: Persistent neurologic deficit and adhesive arachnoiditis following intrathecal 2-chlorprocaine injection. Anesth Analg 59:452–454, 1980
107. Reynolds F, Hargrove RI, Wyman JB: Maternal and foetal plasma concentrations of bupivacaine after epidural block. Br J Anaesth 45:1049–1053, 1973
108. Ritchie JM, Greengard P: On the active structure of local anesthetics. J Pharmacol Exp Ther 133:21–45, 1961
109. Ritchie JM, Ritchie B, Greengard P: The active structure of local anesthetics. J Pharmacol Exp Ther 150:152–159, 1965
110. Ritchie JM, Ritchie B, Greengard P: The effect of the nerve sheath in the action of local anesthetics. J Pharmacol Exp Ther 150:160–164, 1965
111. Rolbin SH, Cole AFD, Hew EM, et al: Prophylactic intramuscular ephedrine before epidural anaesthesia for cesarean section. Efficacy and actions on the foetus and newborn. Can Anaesth Soc J 29:148–153, 1982
112. Rolbin SH, Halpern SH, Braude BM, et al: Fluid through the epidural needle does not reduce complications of epidural catheter insertion. Can J Anaesth 37:337–340, 1990
113. Rosen MA, Boysinger CL, Shnider SM, et al: Evaluation of neurotoxicity after subarachnoid injection of large volumes of local anesthetic solutions. Anesth Analg 62:802–808, 1983
114. Rosenblatt DB, Belsey EM, Lieberman BA, et al: The influence of maternal analgesia on neonatal behavior: II. Epidural bupivacaine. Br J Obstet Gynecol 88:407–413, 1981
115. Salvolaine ER, Pandya JB, Greenblatt SH, et al: Anatomy of the human lumbar epidural space: New insights using CT-epidurography. Anesthesiology 68:217–220, 1988
116. Santos A, Datta S: Prophylactic use of droperidol for control of nausea and vomiting during spinal anesthesia for cesarean section. Anesth Analg 63:85–87, 1984
117. Santos A, Pedersen H, Finster M, et al: Hyperbaric bupivacaine for spinal anesthesia in cesarean section. Anesth Analg 63:1009–1013, 1984
118. Scanlon JW, Brown WV, Weiss JB, et al: Neurobehavioral responses of newborn infants after maternal epidural anesthesia. Anesthesiology 40:121–128, 1974
119. Sevarino F, Johnson M, Lema M, et al: The effect of epidural sufentanil on shivering and body temperature in the parturient. Anesth Analg 4:530–534, 1989
120. Sharkey A, Lipton JM, Murphy MT, et al: Inhibition of postanesthetic shivering with radiant heat. Anesthesiology 66:29–52, 1987
121. Shah JL, Veness AM: Epidural blood patch using a catheter. Diagnosis of an unrecognized dural tap. Anaesthesia 40:1120–1123, 1985
122. Sinclair CJ, Scott DB: Comparison of bupivacaine and etidocaine in extradural blockade. Br J Anaesth 56:1447, 1984

123. Spivey DL: Epinephrine does not prolong lidocaine spinal anesthesia in term parturients. Anesth Analg 64:468–470, 1985
124. Sprague DH: Effects of position and uterine displacement on spinal anesthesia for cesarean section. Anesthesiology 44:164–166, 1976
125. Stevens RA, Chester WL, Schubert A, et al: pH Adjustment of 2-chlorprocaine quickens the onset of epidural anesthesia. Can J Anesth 36:515–518, 1989
126. Thauer R, Simon E: *In* Ito S, Ogata K, Yoshimura A (eds): Spinal Cord and Temperature Regulation Advances in Climatic Physiology. Tokyo, Izako Shoin, 1972, pp 22–49
127. Thompson EM, Wilson CM, Moore J, et al: Plasma bupivacaine levels associated with extradural anaesthesia for caesarean section. Anaesthesia 40:427–432, 1985
128. Thornburn J, Moir DD: Epidural analgesia for elective Caesarean section. Anaesthesia 35:3, 1980
129. Wang BC, Hillman DE, Spielholz N, et al: Chronic neurological deficits and Nesacaine-CE. An effect of the anesthetic, 2-chlorprocaine, or the antioxidant sodium bisulfite? Anesth Analg 63:445–447, 1984
130. Wang JK, Nauss LA, Thomas JE: Pain relief by intrathecally applied morphine in man. Anesthesiology 50:149–151, 1979
131. Webb PJ, James FM, Wheeler AS: Shivering during epidural analgesia in women in labor. Anesthesiology 55:706–707, 1981
132. Workhaven NM: Intravenous fluid temperature, shivering, and the parturient. Anesth Analg 65:86–88, 1986
133. Writer WDR, Dewan DM, James FM III: Three percent 2-chloroprocaine for Caesarean: Appraisal of a standardized dose technique. Can Anaesth Soc J 31:559, 1984
134. Yaksh TL, Reddy SVR: Studies in the primate on the analgetic effects associated with intrathecal actions of opiates, alpha-adrenergic agonists, and beclofen. Anesthesiology 54:451–467, 1981

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EPIDURAL AND SPINAL ANALGESIA
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NEONATAL SPINAL ANESTHESIA

Linda Jo Rice, MD, and John T. Britton, MD

> The advantages to be gained by the use of spinal anaesthesia have so far impressed me that I am convinced that it will occupy an important place in the surgery of children in the future.
>
> TYRELL-GRAY, 1910

August Bier, widely regarded as the father of spinal anesthesia, reported on an 11-year-old boy who underwent debridement of a tuberculous ischial abscess in his 1899 paper on "cocainization of the spinal cord."[6] By May 1900, Bainbridge's[3] report of spinal anesthesia in an infant (repair of a strangulated hernia in a seriously ill 3-month-old infant) had appeared. His report concludes with the statement, "to those present at the operation, it was apparent that a general anesthetic would have proved fatal to the child." This makes sense when one considers that general anesthesia at that time meant chloroform, most likely open drop.

The largest contemporary series of pediatric spinal anesthetics was published in 1909 by Tyrell-Gray,[39] a British surgeon: 300 spinal anesthetics for procedures below the diaphragm. He reported one death in this series, that of a gravely ill child, who appeared to sustain a respiratory arrest secondary to the combination of a high level of spinal anesthesia and parenterally administered morphine. Tyrell-Gray was particularly impressed by the almost total absence of postoperative vomiting as well as by the long duration of postoperative analgesia.

Pediatric spinal anesthesia continued to be popular into the 1940s

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and 1950s as is demonstrated by the observation in 1948 in Leigh and Belton's *Textbook of Pediatric Anesthesia* that 10% of all anesthetics performed in children at Vancouver General Hospital were spinal anesthetics, including lobectomies and pneumonectomies.[25] These pioneer pediatric anesthesiologists also noted that care of the patient following injection of the anesthetic solution into the subarachnoid space is still the most important part of spinal anesthesia.

What happened to alter the popularity of spinal anesthesia in the pediatric surgical population? General anesthesia became more reliable, with the advent in 1944 of neuromuscular blocking agents and development of modern volatile agents, starting with halothane in 1956. However, pediatric spinal anesthetics never disappeared completely. Modern reports include that of Calvert,[11] a British neurosurgeon, who reported in 1966 on a series of 23 cases in which direct spinal anesthesia was employed for repair of myelomeningocele in newborns. Linke and Merin[26] published a series in 1976 in which spinal anesthesia was employed in children for renal transplantation. Melman and coworkers[30] employed spinal anesthesia for numerous pediatric general surgical procedures. Then in 1983, at the American Society of Anesthesiologists Regional Anesthesia Breakfast Panel, Abajian et al[1] started an explosion in modern pediatric spinal anesthesia when they reported on a series of 81 spinal anesthetics performed on 78 infants under 1 year of age.

WHY DO A SPINAL?

We now have modern anesthetic agents and well-trained anesthesiologists caring for children; we no longer need what Bainbridge thought was the advantage of spinal anesthesia in the very ill child. However, in this modern era of high technology, the neonatalogists provide us with new challenges: the 1000 g, 28-week gestation premature infant who just came off extracorporeal membrane oxygenation and now must emergently have incarcerated inguinal hernias repaired; the 42-week postconceptual age infant for "elective" hernia repair; and the 15-month-old oxygen-dependent formerly premature infant, who bears the residual problem of bronchopulmonary dysplasia. As first noted by Steward in 1982,[37] preterm infants are more prone to respiratory complications following general anesthesia than are term infants.[32] Although Welborn et al[40] and others[24, 27] have attempted to pinpoint the precise time during which otherwise healthy premature infants are no longer at increased risk for postoperative apnea, bradycardia, and periodic breathing following general anesthesia, there is still no consensus as to when this increased risk ceases. Many of us who frequently use spinal anesthesia for high-risk infants believe that the postoperative apnea risk is lower with this technique if no adjunct sedation is employed.

Premature nursery graduates and children less than 1 year of age are not the only surgical candidates who may benefit from a spinal anesthetic. There are older pediatric patients in whom one may wish to avoid instrumentation of the airway, such as those patients who have recently undergone tracheoplasty, or who have known subglottic stenosis. There are also children with pulmonary diseases such as cystic fibrosis or severe asthma, or patients with stable neuromuscular diseases such as muscular dystrophy who may benefit from a spinal anesthetic with minimal sedation for procedures below the diaphragm. Sometimes parents or older children request alternatives to general anesthesia. Spinal anesthesia may be ideal for such children.

ANATOMIC CONSIDERATIONS

There are several important anatomic differences between the spinal canal of the infant and that of the adult (Fig. 1). The neonatal spinal cord can end anywhere from T12 to L3; lower than the normal level in adults. Therefore, it is preferable to perform the lumbar puncture at the L4 or L5 interspace. At that level, the approximate

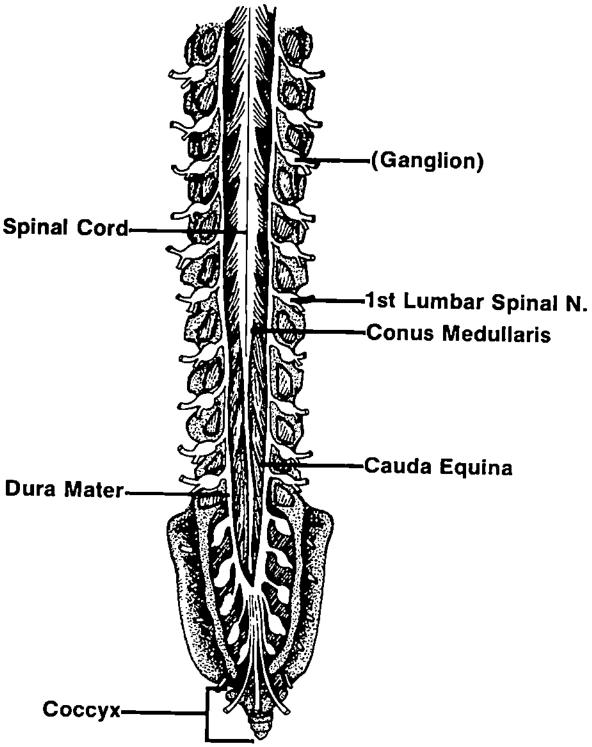

Figure 1. Lumbosacral spine and spinal cord in the newborn. (*From* Broadman LM: Regional anesthesia for the pediatric outpatient. Anesth Clin North Am 5:57, 1987; with permission.)

depth of the subarachnoid space is 1 to 1.5 cm from the skin. Busoni and Messeri[10] recently reviewed 500 lateral and anteroposterior radiographs of the lumbar spine in children aged 1 day to 16 years. They noted that the intercristal line crosses the midline at the level of the fifth lumbar vertebra in children, and even lower, at L5–S1 in neonates.[10] The volume of CSF in the term newborn is approximately 50 mL, compared with 140 mL in adults.[31] These values will vary, of course, for older children.

TECHNICAL TIPS: METICULOUS ATTENTION TO DETAIL IS CRUCIAL

Equipment needed for a neonatal anesthetic includes a standard adult spinal anesthesia tray, a 1-mL tuberculin syringe, and a 22-gauge, 3.5-cm or 25-gauge, 2.25-cm pediatric Quincke needle. With the availability of styletted Quincke needles appropriately sized for these small infants, there is no reason to risk iatrogenic intraspinal epidermoid tumor by employing an unstyleted needle.[4, 36] Becton-Dickinson manufactures both sizes of needles with clear hubs. At the time of writing, the only tray manufactured specifically for pediatric spinal anesthesia, with all equipment appropriately sized, is produced by Preferred Medical Products of Canada (800-267-2664). A clear, fenestrated operative drape is useful following skin preparation; this enables the operator to observe the infant during block placement while maintaining a sterile surface below the infant. Additional useful tools include ½- or 1-inch roller gauze with which to restrain the infant's upper extremities following the block, as well as a cap (such as stockingette) to assist in keeping the infant warm. Performance of the block will require two assistants: one securely restrains the infant while the second comforts the infant and tends the airway, keeping the pacifier in place.

The block is performed with the patient in the lateral or sitting position, with the back maximally flexed and the head extended (Figs. 2 and 3). It is important that the neck of the infant remains extended while the spinal anesthetic is placed; Gleason et al[20] have shown that flexion of the neck of a preterm infant may decrease the transcutaneous P_{O_2} by as much as 28 mm Hg. The assistant holding the patient in position must restrain him firmly, as a squirming patient will markedly increase the difficulty of the lumbar puncture.

It should be remembered that performance of a diagnostic lumbar puncture on the pediatric ward is usually delegated to the pediatric intern, with an experienced nurse holding the child. The "holder" will make the "doer" look good, or complicate the procedure unbearably. The novice operator in a small hospital might look to a pediatric colleague or an experienced pediatric nurse to hold the child.

The operator places his nondominant hand so that the little finger locates the iliac crest; the appropriate interspace is then located with

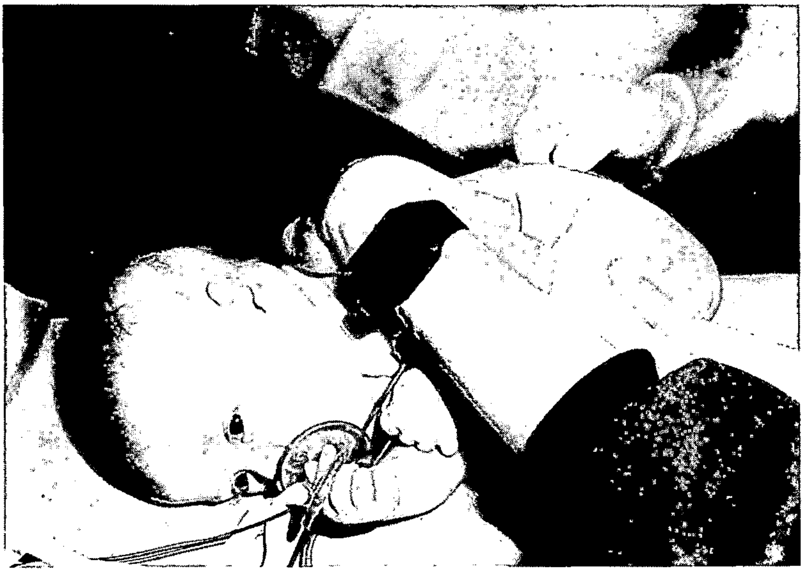

Figure 2. Position of an infant for lumbar puncture. Note that the neck must remain extended to maintain airway patency. (*From* Rice LJ, Hannallah RS: Local and regional anesthesia. *In* Motoyama EK, Davis PJ (eds): Smith's Anesthesia for Infants and Children, ed 5. St. Louis, CV Mosby, 1990, p 398; with permission.)

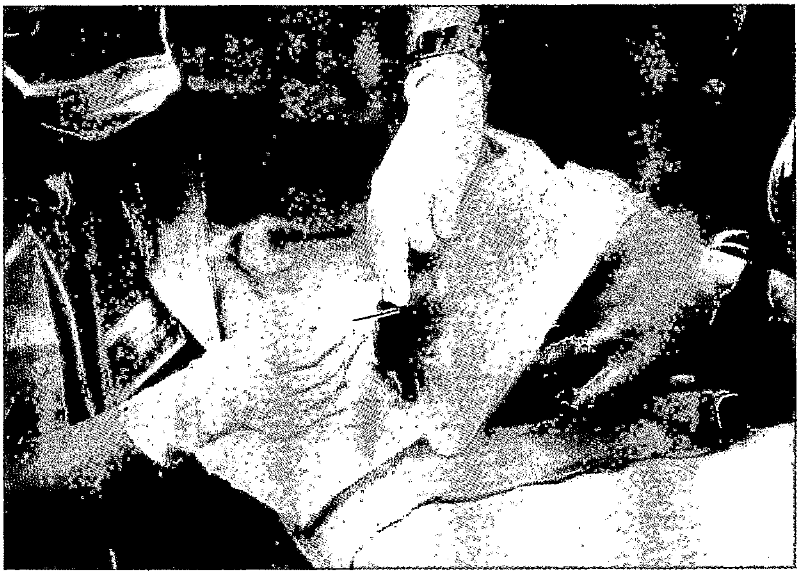

Figure 3. Successful lumbar puncture is confirmed by the free flow of CSF. The needle is enhanced for greater clarity. (*From* Rice LJ, Hannallah RS: Local and regional anesthesia. *In* Motoyama EK, Davis PJ (eds): Smith's Anesthesia for Infants and Children, ed 5. St. Louis, CV Mosby, 1990, p 398; with permission.)

the second and third fingers. This will also allow the operator to assist the colleague who is controlling the buttocks of the infant.

The Quincke needle is inserted with the dominant hand, usually employing a midline approach, parallel to the floor and angled toward the umbilicus. Bloody taps will occur if the needle is not advanced exactly in the midline. Entry into the lumbar subarachnoid space is usually signaled by a sudden "give" of the posterior spinal ligaments, followed by a similar feeling as the dura is punctured. These "pops," however, may be less distinct in the preterm infant.

The use of a 22-gauge needle allows brisk, free flow of CSF; free flow is less exuberant with the 25-gauge needle. Once CSF has been demonstrated, the tuberculin syringe containing the appropriate volume of local anesthetic is carefully attached and secured to the spinal needle. A very small volume of CSF may be aspirated before injection or one may simply inject the local anesthetic solution. One must realize that the volumes involved here are quite small; inattention to the details of "mating" the tuberculin syringe to the hub of the Quincke needle will result in loss of local anesthetic fluid on injection and a level of spinal anesthesia inadequate for the surgery.

It is recommended that the operator carefully support the needle with the nondominant hand while injecting with the dominant (just as when performing a spinal anesthetic in an older patient). Neonatal spinal anesthesia is a game of millimeters; if the needle is not well stabilized, all of the anesthetic solution may not be placed in the subarachnoid space, and central neuraxis blockade may be incomplete.

Abajian et al[1] recommend that the needle be left in position for 5 seconds after the local anesthetic has been injected in order to prevent the drug from tracking back to the skin puncture following removal of the needle. They believe that a substantial volume of local anesthetic injected may be lost through the skin puncture if the anesthesiologist does not take time to allow the local anesthetic to mix with the CSF before withdrawing the needle.

Once the Quincke needle is removed, the patient is immediately placed in the supine position. Motor blockade should be evident within 1 to 2 minutes. It is imperative that the patient's feet should not be placed higher than his head; specifically, one should not lift the infant's legs to place an electrocautery grounding pad on his back. "High spinals" occur with such position changes.[2, 42]

It is important to log roll the infant or lift him or her as a unit should the need for position changes arise. On the other hand, if the level of anesthesia seems to be lower than desired, placing the patient in the head-down position for 10 to 20 seconds will certainly raise the level of spinal anesthetic. A recent report reinforces the fact that performance of the lumbar puncture is not the most important part of the technique; meticulous patient monitoring is critical. Wright and colleagues[42] report four high-risk neonates undergoing spinal anesthesia for inguinal hernia repair. Two of their infants demonstrated high spinal blocks following lifting of legs for electrocautery grounding pad placement; however, the other two received moderate doses of subarachnoid tetracaine (0.5–0.6 mg/kg) and demonstrated weak cries and poor upper extremity movement even though meticulous attention was given to patient position. One of these infants developed bradycardia and hypotension that immediately responded to atropine. The authors discuss the absolute need for meticulous attention to detail, including close monitoring of high-risk newborns undergoing spinal anesthesia and restate the fact that this technique, although valuable, is no more risk-free than any other anesthetic technique.

In an infant or young child, the intravenous catheter may be placed in a lower extremity after the spinal anesthetic has been administered rather than struggling with attempts at venipuncture in order to provide fluid loading before establishing the block. Dohi et al[15] noted that patients less than 5 years of age show little or no change in blood pressure with spinal anesthesia, even without fluid loading. In their series, children older than 6 years of age who underwent spinal anesthesia to the T4 level without fluid loading demonstrated the same widely variable decreases in blood pressure that adults did (Fig. 4). Dohi et al attributed these age-related differences partly to immature development of the sympathetic nervous system in small children. They also noted the wide variation in doses between infants and adults and speculated that this may relate to physical and physiologic differences among infants, children, and adults, including the amount of CSF, diameter and surface area of the spinal cord and nerve roots, and rate of absorption of local anesthetics from the subarachnoid space.[16] These factors may also contribute to the relatively larger milligram per kilogram doses and shorter duration of spinal anesthesia seen in infants as compared with adults.

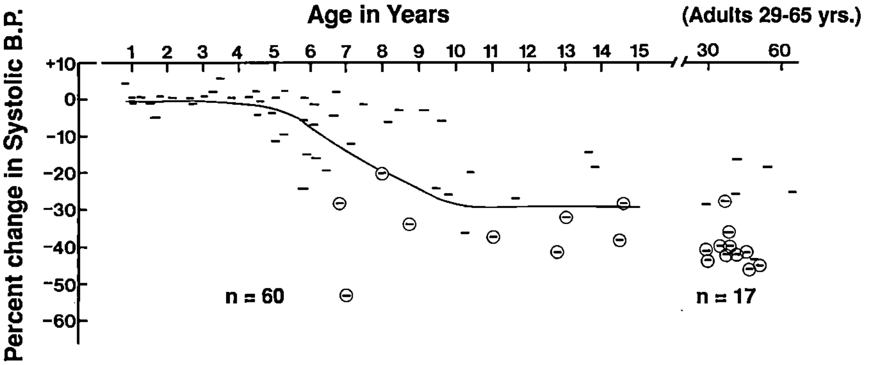

Figure 4. Scattergram of percentage changes in systolic blood pressure from control plotted versus age in years. – = maximal percentage change in systolic blood pressure following spinal anesthesia. ⊖ = a case in which a pressor agent was given to prevent a further decrease in blood pressure. (*From* Dohi S, Naito H, Takahashi T: Age-related changes in blood pressure and duration of motor block in spinal anesthesia. Anesthesiology 50:320, 1979; with permission.)

Abajian and Rice have performed over 900 spinal anesthetics for children less than 1 year of age, with no fluid loading, no hypotension, and no bradycardia (JC Abajian, MD, personal communication, 1991). Of course, fluid loading should be employed for children older than 6 years of age.

A soothing touch and a pacifier or "whiskey nipple" are usually all that an infant less than 52 weeks postconceptual age and still at risk for apnea requires to remain quiet during surgery (Fig. 5). It should be remembered that a spinal anesthetic does not provide motor control of the infant's upper extremities, and that a crying infant with arms waving will not provide adequate surgical conditions even if the anesthetic level is adequate. Therefore, appropriate upper extremity restraint and maintenance of a quiet infant are important components of this anesthetic technique. Placement of the blood pressure cuff on the infant's lower extremity following placement of the block eliminates the problem of a sleeping youngster being awakened by repeated cuff inflations.

Sedation should be used with care, realizing that use of adjunct sedative agents may remove the benefit of the regional technique. Just as in the adult patient, use of sedative agents should be guided by the overall medical status of the pediatric patient, as well as recognition of the pharmacology of such drugs in the neonatal age group. It should be emphasized that although those of us experienced in spinal anesthesia for the high-risk infant believe that if no sedation is employed,

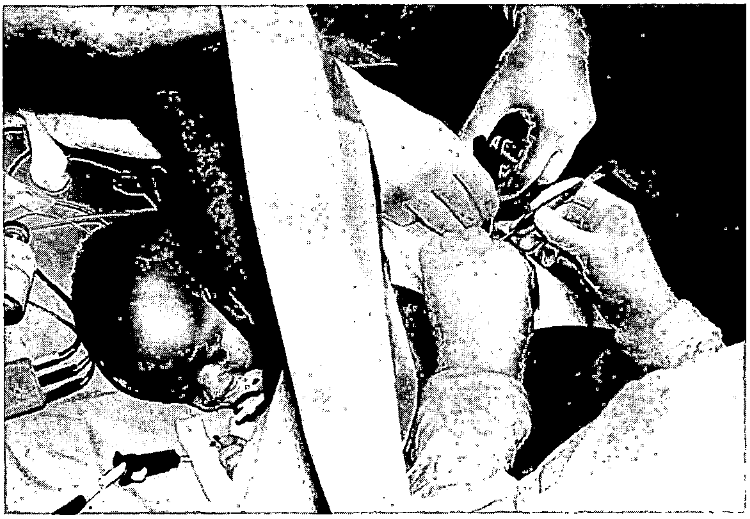

Figure 5. Often, a soothing touch and a pacifier are all that the infant needs to remain calm during surgery. Sometimes intravenous or inhalation supplementation are needed. (*From* Rice LJ, Hannallah RS: Local and regional anesthesia. *In* Motoyama, Davis (eds): Smith's Anesthesia for Infants and Children, ed 5. St. Louis, CV Mosby, 1990, p 401; with permission.)

there is no additional risk of apnea above the infant's baseline risk, there is only one randomized study completed at this time to confirm this belief.[41]

Welborn and colleagues,[41] in a prospective, randomized study of general versus spinal anesthesia for hernia repair in high-risk neonates, found that although spinal anesthesia alone did not appear to place the infant at risk for postoperative apnea, addition of ketamine sedation caused 90% of the patients to develop prolonged apnea or apnea and bradycardia. Therefore, infants at risk should still be monitored in the hospital overnight, and use of ketamine should be avoided in neonates at risk for apnea.

There is no information available regarding safety of other sedative agents with spinal anesthesia in this age group, although N_2O, methohexital, and even ketamine have been successfully employed in some of the series mentioned in this article.

WHICH DRUG SHOULD BE USED?

Until the 1950s, amethocaine (2.5%) and lidocaine (4%) were the drugs most commonly used for spinal anesthesia in children.[25] Although hyperbaric tetracaine, introduced by Berkowitz in 1951, has now become the agent of choice, lidocaine and bupivacaine are still in use.[2, 5] The choice of local anesthetic agent should be made based on the projected length of surgery. It does appear, however, that spinal anesthetics do not last as long in infants and children as they do in adults.[15, 32, 34]

Although isobaric tetracaine and bupivacaine have been used outside the United States, most experience in this country is with the same hyperbaric tetracaine solution popularly employed in adults. At Children's National Medical Center, the most common solution employed is hyperbaric tetracaine with epinephrine. The minimum dose employed is 1 mg. This sample dose would be prepared as follows: epinephrine 1:1000, 0.02 mL (a syringe wash) is drawn into a disposable tuberculin syringe to which 0.2 mL of tetracaine, 1%, and 0.2 mL of dextrose, 10%, are added. The amount of drug required for the block is calculated and the excess discarded. There is no need to include the dead space of the needle in the calculations.

The level of anesthesia obtained in a child less than 1 year of age by doses ranging from 0.3 to 1.2 mg/kg of tetracaine is almost uniformly T4 unless the patient is placed in the Trendelenburg position after performance of the block. The major variation is in length of block; larger doses provide longer periods of anesthesia, particularly in infants weighing less than 1200 g (CB Berde, MD, personal communication, 1991).

Both lidocaine and bupivacaine are prepared in a similar fashion; however, as these drugs are supplied in hyperbaric form, no dextrose is added. Epinephrine may be added to either of the latter solutions to prolong the length of the block.

CONTEMPORARY CLINICAL EXPERIENCE WITH NEONATAL SPINAL ANESTHESIA

In 1977, Abajian et al[1] began to offer spinal anesthetics both to high-risk neonates and to full-term infants whose parents requested it for surgery below the umbilicus. They reported in 1984 on a series of 81 spinal anesthetics in 78 infants. Thirty-six of these were categorized as high-risk infants because they had been premature or because they had been treated for neonatal respiratory distress. They found that with a dose of 1 mg of hyperbaric tetracaine/epinephrine for the small patients, and 2 mg for the big ones, all infants had a level of spinal anesthesia at or below T4. In this initial series, 60 patients received spinal anesthetics that were successful on the first attempt, ten required a second attempt, and spinal anesthesia was abandoned in eight term infants because of inability to obtain CSF. Supplementation was employed in 14 anesthetics because of inadequate levels of spinal anesthesia in six and because the duration of the surgery outlasted the anesthetic in seven patients. Abajian's 13-year experience now exceeds 500 patients less than 1 year of age, with no major morbidity and no mortality. No patient has required intubation for a high spinal anesthetic, and no patient has required treatment for hypotension. Surgical procedures performed under spinal anesthesia range from inguinal hernia repair to colostomy for imperforate anus. They continue to believe that spinal anesthesia is a safe and reliable anesthetic in both high-risk and normal infants, but concede that the superiority of spinal to other forms of anesthesia in this group of patients remains to be demonstrated.

Harnik and coworkers[22] evaluated spinal anesthesia in premature infants recovering from respiratory distress syndrome. They studied 20 infants with a gestational age of less than 36 weeks, who underwent inguinal hernia repair between the 35th and 78th postconceptual week of life. All suffered from severe respiratory distress syndrome. Eleven patients were less than 44 weeks postconceptual age and eight were under 2500 g of weight at time of surgery. Doses varied from 0.24 to 0.65 mg/kg of hyperbaric tetracaine without epinephrine, with infants under 3000 g of weight receiving the larger doses. Oxygen and nitrous oxide were used for sedation in some infants during the lumbar puncture, while supplementation using ketamine, mask halothane, or local injection of lidocaine was required in eight patients. Five of these patients received what was later concluded to be an inadequate dose of tetracaine.

One infant with a history of frequent apnea had an episode of apnea and bradycardia following injection of the tetracaine; he was intubated for the procedure and extubated at the close of surgery. The only postoperative complication was apnea occurring 8 hours following completion of surgery in a patient with a temperature of 34.2°C. Intubation and 24 hours of ventilation were required in this child. Somatosensory evoked potentials were performed in eight infants, with latencies noted to increase during the time of motor block, and to be back to normal by 3 hours after the block, along with full return of motor function. These authors concluded that although subarachnoid blockade may avoid the increased incidence of postoperative respiratory complications associated with general anesthesia and reduce the requirement for postoperative mechanical ventilatory support, it does not change the need for intensive postoperative monitoring in these high-risk infants.

Blaise and Roy[7] reported on 34 patients aged 7 weeks to 13 years who received spinal anesthesia for minor abdominal or orthopedic procedures. The older childen received diazepam premedication, whereas those under 2 years of age received intravenous sedation including diazepam, 0.1 mg/kg, and/or fentanyl, 1 to 2 μg/kg. Four of 34 patients required general anesthesia because of inability to obtain CSF. In the remaining 30 patients, the dose of isobaric tetracaine varied from 0.2 to 0.5 mg/kg and that of hyperbaric bupivacaine 0.75% from 0.3 to 0.4 mg/kg. The level of block varied from T12 to T4. Intravenous lines were placed before placement of the spinal block, and 6 mL/kg of lactated Ringer's solution was infused during the preparation and administration of the spinal anesthetics.

Supplementation of spinal anesthesia varied between the orthopedic and the abdominal surgery groups. Six of 18 orthopedic patients required sedation, whereas five required general anesthesia because the length of the surgery exceeded the duration of the spinal anesthetic. In the lower abdominal surgery group, 6 of 12 patients required sedation, whereas six received a light general anesthetic because of inadequate relaxation or peritoneal retraction pain. One 2½-year-old patient who received a lumbar puncture with a 22-gauge needle suffered a postspinal anesthetic headache that resolved with increased fluid administration. Blaise and Roy[7] concluded that when skilled personnel are available in combination with knowledgeable assistants, the results of subarachnoid block are generally satisfactory. When any of these factors are absent, the technique will probably fail.

Rice and colleagues[34] studied the duration of spinal anesthesia in patients less than 1 year of age using three different drugs. They employed a standardized regimen of each drug and observed the time from first injection of local anesthetic solution to the first movement of toes. Tetracaine was used in a dose of 0.4 mg/kg, either with or without epinephrine, while hyperbaric lidocaine and epinephrine were used in a dose of 3 mg/kg. No infant was sedated for performance of the block, and no sedation was used until the block level had been recorded, using a peripheral nerve simulator set to tetanus as a sensory stimulus. All surgery was below the diaphragm, and all anesthetics provided adequate surgical anesthesia to the T4 level. As in Abajian's study, intravenous catheters were placed following induction of spinal anesthesia, and no episode of hypotension or bradycardia was noted. Atropine was not routinely given in this study. These authors conclude that lidocaine with epinephrine is suitable for surgeries expected to last about 30 minutes, whereas plain hyperbaric tetracaine is preferred for

60 minutes of surgery, and tetracaine with epinephrine provides 90 minutes of surgical anesthesia.

Mahe and Ecoffey[29] used isobaric bupivacaine 0.5%, either alone or in combination with epinephrine 1:200, 000, for spinal anesthesia in 28 infants less than 6 months of age undergoing inguinal hernia repair. Doses varied according to the weight of the infant, with 1.25 mg employed for infants weighing less than 2 kg, 3.75 mg for those between 2 and 5 kg, and 5 mg for those above 5 kg. The duration of motor blockade did not vary significantly between the two groups, with the mean duration of motor blockade lasting 70 minutes when epinephrine was not added to the local anesthetic solution, and 81 minutes when it was. Four infants had a decrease in systolic blood pressure greater than 40%, which responded to a bolus of lactated Ringer's solution. However, the hemodynamic changes witnessed in this study are probably due to recorded control values for heart rate and arterial blood pressure that are higher than normal values. Blood pressure measurements obtained following placement of the spinal anesthetic are within normal limits, as opposed to the hypertensive values recorded in the preoperative period. No patient was premedicated before placement of the block. The authors believed that this local anesthetic regimen did provide efficacious and safe spinal anesthesia for infants less than 6 months of age.

Gallagher and Crean[18] successfully employed hyperbaric bupivacaine 0.5% in a dose of 0.3 mg/kg for inguinal hernia repair in a group of 25 high-risk premature infants, but did not report the duration of the anesthetic. Parkinson and coworkers[32] used hyperbaric 0.75% bupivacaine with epinephrine in a dose of 0.6 mg/kg for surgery below the umbilicus in a group of infants less than 8 months of age, with a mean duration of anesthesia of 84 ± 16 minutes.

In summary, many different drugs and doses are in use at this time. It is suggested that the original articles be consulted before selecting agents and doses for your practice. It should also be noted that most contemporary experience with pediatric spinal anesthesia is in infants less than 1 year of age; consequently, doses for older children are not as well defined. There is a learning curve as with any new technique; success will improve with experience.

WHAT ELSE DO WE KNOW?

Pascucci and coworkers[33] investigated the effects of spinal anesthesia on chest wall displacements in seven unpremedicated infants less than 45 weeks conceptual age, undergoing inguinal hernia repair. A hyperbaric solution of tetracaine, 1 to 1.2 mg/kg with 40 μg of epinephrine, was employed, and 30 seconds of tidal breathing was recorded before and following induction of spinal anesthesia to the T2–4 level. Spinal anesthesia had no effect on respiratory rate or heart rate, although systolic blood pressure did decrease by 10% as compared with baseline. Before spinal blockade, the rib cage moved outward during inspiration in six of seven infants. Spinal anesthesia deceased inspiratory movement of the rib cage in all six of these infants and induced paradoxic (inward) rib cage movement during inspiration in four of the six infants. They concluded that in supine awake infants, the inspiratory muscles of the rib cage serve to stabilize and inflate the thorax.

Rice and colleagues[35] investigated transcutaneous CO_2 levels during spinal anesthesia in 15 high-risk neonates undergoing inguinal hernia repair and found that there was no significant increase in transcutaneous CO_2 in spite of sensory blockade to the T4 level. Pulse oximetry demonstrated no change in oxygenation in these infants. All of the infants were on apnea monitors; two were on home oxygen and eight had resting TCO_2 levels greater than 40 before performance of the subarachnoid block.

Britton[9] is developing an animal model to study the effects of local anesthetics on the developing spinal cord. By both clinical and somatosensory evoked potential monitoring, the placement of local anesthetics in the neonatal spinal or caudal epidural space provides reversible neural blockade similar to that seen in adults.[22] However, there are no studies available to confirm this in animal models at this time.

Spinal anesthesia has also been compared with caudal anesthesia in the same high-risk group of premature infants and premature graduates.[21, 23] Authors of these series conclude that safety of caudal anesthesia may be similar to spinal anesthesia.

WILL A SPINAL WITH NO SEDATION GUARANTEE NO APNEA POSTOPERATIVELY?

Cox and Goresky[14] recently reported two cases of life-threatening apnea in premature infants following spinal anesthesia for inguinal hernia repair. One of these infants had severe bronchopulmonary dysplasia and was on home oxygen. Although he received oral theophylline, he still averaged one to two self-limited periods of apnea and bradycardia per day. Following the surgery, while in the intensive care unit, he was administered oral codeine for postoperative analgesia. Fourteen hours postoperatively he required intubation for increasing episodes of apnea and bradycardia unresponsive to intravenous naloxone. He required 5 days to be extubated successfully. The second premature infant (25 weeks gestation; now 38 weeks postconceptual age) also had severe bronchopulmonary dysplasia requiring oxygen and oral theophylline and was anemic. He had no apneic episodes during the first 24 hours following surgery, but demonstrated apneic episodes beginning at 32 hours, at which time he was noted to be hypothermic to 34°C and his hemoglobin had fallen to 7.1 g/100 mL. He eventually required intubation for 2 days and demonstrated signs of sepsis.

Both of these infants were not "healthy premies" but had serious underlying medical disease. Indeed, the authors of the report specifically exonerate the spinal anesthetics as a precipitating factor in the perioperative complications of these complicated neonates.

It should be noted that there are at least two reports in the literature of term infants demonstrating apneic episodes following uneventful general anesthesia.[13, 38] These case reports only serve to remind us that there is no such thing as a risk-free anesthetic, and there is no substitute for vigilant postoperative monitoring. Thus, we still recommend overnight respiratory monitoring for the uncomplicated high-risk premature undergoing inguinal hernia repair, even if the infant receives an unsupplemented spinal anesthetic.

WHAT ABOUT HEADACHES?

Postlumbar puncture headaches (PLPH) are a rare occurrence in the pediatric population. Diagnostic lumbar puncture is among the most common procedures performed on infants in the nursery or emergency room, and there are no case reports of posture-associated increased irritability following lumbar puncture in this population. Although both investigators routinely ask parents about changes in mood or feeding habits following spinal anesthesia in infants, neither Abajian nor Rice have noted any PLPH in their patients. It is of interest that both investigators have performed multiple spinal anesthetics in infants undergoing repeated surgeries, with no apparent PLPH and with parental satisfaction.

Children do, however, readily complain of headaches. Indeed, it is one of the most common chronic somatic complaints in the pediatric age group. Fernbach[17] reported that he had not observed PLPH in children in 20 years of pediatric oncology experience. Blaise and Roy[7] believe that a 2½-year-old boy suffered PLPH following spinal anesthesia in their series. There are a few case reports of epidural blood patches providing effective treatment following PLPH.[8, 19, 28] In each instance, needles larger than 20 gauge were used to perform myelography or diagnostic spinal tap.

One prospective study of cancer patients undergoing lumbar puncture for placement of chemotherapeutic agents followed 26 children aged 3 to 17 years, who underwent 36 lumbar punctures.[8] Daily questionnaires were completed by the patient and parent for 5 days following lumbar puncture with a 20-gauge needle. These investigators found that PLPH was significantly more frequent in children older than 13 years, but that even these children usually were headache-free after 48 hours. No child in this series required epidural blood patch for PLPH.

SUMMARY

Spinal anesthesia has been practiced in pediatric patients for roughly the same period of time that it has been used in adults. Many different drugs and dosages have been successfully employed, and it appears that spinal anesthesia without sedation may offer real advantages in the premature infant at high risk for postanesthetic apnea. However, avoidance of general anesthesia will not guarantee that a neonate with multiple medical problems will not evidence apnea or other difficulties in the postoperative period, and it is still recommended that postoperative respiratory monitoring be employed in an inpatient setting.

The popularity of spinal anesthesia for the "little folk" varies as the wheel of anesthetic practice revolves and the clinical challenges facing the practitioner alter. However, as Corning noted in his early report of a therapeutic cocaine spinal anesthetic, "Whether the method will ever find an application as a substitute for etherization in genito-urinary or other branches of surgery, further experience alone can show. Be the destiny of the observation what it may, it has seemed to be, on the whole, worth recording."[12]

References

1. Abajian JC, Mellish RWP, Browns AF, et al: Spinal anesthesia for surgery in the high risk infant. Anesth Analg 63:359–362, 1984
2. Bailey A, Valley R, Bigler R: High spinal anesthesia in an infant [letter]. Anesthesiology 70:560, 1989
3. Bainbridge WS: Analgesia in children by spinal injection, with a report of a new method of sterilization of the injection fluid. Medical Record 58:937–940, 1900
4. Batnitzky S, Keucher TR, Mealey J: Iatrogenic intraspinal epidermoid tumors. JAMA 237:148–150, 1977
5. Berkowitz S, Greene BA: Spinal anesthesia in children: Report based on 350 patients under 13 years of age. Anesthesiology 12:376–387, 1951
6. Bier A: Versuche uber cocainisrung des ruchenmarkes. Dtsch Z Chirurg 51:361–369, 1899
7. Blaise GA, Roy WL: Spinal anaesthesia for minor paediatric surgery. Can Anaesth Soc J 33:227–230, 1984
8. Bolder PM: Postlumbar puncture headache in pediatric oncology patients. Anesthesiology 65:695–698, 1986
9. Britton JT: Neurotoxicity of local anesthetics. *In* Animal Pain and Its Control. New York, Churchill Livingstone, in press
10. Busoni P, Messeri A: Spinal anesthesia in children: Surface anatomy. Anesth Analg 68:418–419, 1989
11. Calvert DG: Direct spinal anaesthesia for repair of myelomeningocele. Br Med J 2:86–87, 1966
12. Corning JL: Spinal anaesthesia and local medication of the cord. NY Med J 12:483–485, 1885
13. Coté CJ, Kelly DH: Postoperative apnea in a full-term infant with a demonstrable respiratory pattern abnormality. Anesthesiology 72:559–561, 1990
14. Cox RG, Goresky GV: Life-threatening apnea following spinal anesthesia in former premature infants. Anesthesiology 73:345–347, 1990
15. Dohi S, Naito H, Takahashi T: Age related changes in blood pressure and duration of motor block in spinal anesthesia. Anesthesiology 50:319–323, 1979
16. Dohi S, Seino H: Spinal anesthesia in premature infants: Dosage and effects of sympathectomy. Anesthesiology 65:559–560, 1986
17. Fernbach DJ: Headache after lumbar puncture. Lancet 2:529, 1981
18. Gallagher TM, Crean PM: Spinal anaesthesia in infants born prematurely. Anaesthesia 44:434–436, 1989

19. Ghia JN, Spielman FJ, Steiber SF: The diagnosis and successful treatment of post-lumbar puncture headache in a pediatric patient. Reg Anesth 9:102–105, 1984
20. Gleason CA, Martin RJ, Anderson JV, et al: Optimal position for a spinal tap in preterm infants. Pediatrics 71:31–35, 1983
21. Gunter JB, Gunn CM, Bower RJ, et al: Caudal epidural anesthesia in sixty-nine conscious premature and high-risk infants. Anesthesiology 73:1097, 1990
22. Harnik EV, Hoy GR, Potolicchio S, et al: Spinal anesthesia in premature infants recovering from respiratory distress syndrome. Anesthesiology 64:95–99, 1986
23. Kataria B, Ved S, Harnik E: Spinal versus caudal anesthesia in premature infants recovering from respiratory distress syndrome. Anesthesiology 71:1018, 1989
24. Kurth CD, Spitzer AR, Broennle AM, et al: Postoperative apnea in preterm infants. Anesthesiology 66:483–488, 1987
25. Leigh MD, Belton MK: Pediatric Anesthesia. New York, Macmillan, 1948, pp 120–129
26. Linke CL, Merin RG: A regional anesthetic approach for renal transplantation. Anesth Analg 55:69–73, 1976
27. Liu LMP, Coté CJ, Goudsouzian NG, et al: Life-threatening apnea in infants recovering from anesthesia. Anesthesiology 59:506:510, 1983
28. Lund PC: Reflections upon the historical aspects of spinal anesthesia. Reg Anesth 8:89–97, 1983
29. Mahe V, Ecoffey C: Spinal anesthesia with isobaric bupivacaine in infants. Anesthesiology 68:601–603, 1988
30. Melman E, Penuelas J, Marrufo J: Regional anesthesia in children. Anesth Analg 54:387–390, 1975
31. Menkes JH: Textbook of Child Neurology, ed 3. Philadelphia, Lea & Febiger, 1985, pp 540–543
32. Parkinson SK, Little WL, Malley RA: Use of hyperbaric bupivacaine with epinephrine for spinal anesthesia in infants. Reg Anesth 15:86–88, 1990
33. Pascucci RC, Hershenson MB, Sethna NF, et al: Effect of spinal anesthesia on chest wall displacement in infants. Anesthesiology 69:A773, 1988
34. Rice LJ, DeMars PD, Crooms J, et al: Duration of spinal anesthesia in infants under one year of age: Comparison of three drugs. Anesth Analg 66:S148, 1987
35. Rice LJ, Bacon G, Newman K: Spinal anesthesia does not compromise ventilation or oxygenation in high risk infants. Anesthesiology 71:A1021, 1989
36. Shaywitz BA: Epidermoid spinal cord tumors and previous lumbar punctures. J Pediatr 80:638–640, 1972
37. Steward DJ: Preterm infants are more prone to complications following minor surgery than are term infants. Anesthesiology 56:304–306, 1982
38. Tetzlaff JE, Annand DW, Pudimat MA, et al: Postoperative apnea in a full-term infant. Anesthesiology 69:426–428, 1988
39. Tyrell-Gray H: A study of spinal anaesthesia in children and infants. Lancet 3:913–917, 1909
40. Welborn LG, Ramirez N, Oh TH, et al: Postanesthetic apnea and periodic breathing in infants. Anesthesiology 65:658–661, 1986
41. Welborn LG, Rice LJ, Hannallah RS, et al: Postoperative apnea in former preterm infants: Prospective comparison of spinal and general anesthesia. Anesthesiology 72:834–842, 1990
42. Wright TE, Orr RJ, Haberkern CM: Complications during spinal anesthesia in infants: High spinal blockade. Anesthesiology 73:1290–1292, 1990

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INTRASPINAL OPIOID ANALGESIA IN THE PERIOPERATIVE PERIOD

L. Brian Ready, MD, FRCP(C)

Dramatic pain relief following intraspinal administration of opioids (by both the intrathecal and epidural routes) was first reported in 1979. Experience with the technique exploded in the ensuing decade. Outstanding pain relief and improved status of postoperative patients has been demonstrated consistently. However, rare reports of complications, in particular respiratory depression, have made some practitioners reluctant to use the techniques.

Over the past decade, research and clinical experience has led to knowledge and understanding that has resulted in changes in practice using intraspinal opioid analgesia (IOA). Criteria for patient selection have started to evolve. Lower doses of opioids, especially in elderly or frail patients, are now used. The importance of nurse education, regular medical follow-up, and organized programs directed by anesthesiologists to provide effective and safe analgesia are now recognized. The clinical features of respiratory depression have been clarified, permitting the development of effective, inexpensive bedside monitoring strategies. Polypharmacologic approaches are being used to eliminate some of the problems associated with the use of intraspinal opioids alone.

New practices such as IOA take considerable time to assume their rightful place in clinical practice. Among the last of the important elements to be recognized is that of appropriate compensation to the practitioners offering the care. There are encouraging signs that such recognition is now occurring.

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In 1979, Wang et al[33] reported remarkable pain relief using subarachnoid morphine in cancer patients, while in the same year Behar et al[1] achieved the same result injecting the drug into the epidural space. Subsequent authors have confirmed that selective, long-duration analgesia was possible using these techniques in a variety of clinical settings. However, it soon became clear that a number of side effects might be expected, ranging from annoying (sedation, pruritus, nausea, vomiting, or urinary retention) to life-threatening (early and delayed respiratory depression). A great deal has been learned since that early experience. It is now apparent that with attention to patient selection, appropriate choice of drugs and their dosage, adequate patient monitoring, and effective treatment of side effects, the benefits of IOA can be obtained with a high degree of safety.

WHEN TO USE INTRASPINAL OPIOID ANALGESIA

Benefits of Intraspinal Opioid Analgesia

Several reports regarding the use of epidural opioids for postoperative pain control are of special note. Stenseth et al[31] published a prospective report of the efficacy and side effects of epidural morphine in 1085 patients after thoracic, abdominal, urologic, or orthopedic surgery. This large experience from a single institution provides a wealth of observations that are instructive to the clinician contemplating the use of epidural opioids.

In a randomized, double-blinded study by Rawal et al[23] of obese patients undergoing gastroplasty for weight reduction, the effects of intramuscular and epidural morphine were compared with respect to analgesia, ambulation, gastrointestinal motility, early and late pulmonary function, duration of hospitalization, and occurrence of deep vein thrombosis in the postoperative period. With a protocol designed to provide adequate analgesia by either route, the average dose of intramuscular morphine was up to seven times greater than that required by the epidural route. Patients receiving epidural morphine reported superior analgesia, ambulated sooner, had fewer pulmonary complications, had earlier return of bowel function, and were discharged from hospital earlier than patients receiving intramuscular morphine.

Yeager et al[34] randomized high-risk surgical patients to two groups: the first received general anesthesia and conventional postoperative analgesia (i.e., intramuscular or intravenous opioids), whereas the second group received combined epidural/general anesthesia and epidural opioids for postoperative pain. Mortality, overall complication rate, infection rate, time to extubation, and hospital costs were significantly lower in the epidural group.

Although not as effective as regional analgesia, with local anesthetics for controlling pain associated with vaginal delivery, spinal opioids for control of pain following cesarean section are widely used.

These may be offered when spinal or epidural anesthesia is chosen for surgery. Although most reports focus on the latter application, good results also have been reported using the subarachnoid route.[3] Pain after vaginal delivery originating from a large episiotomy or perineal tear may also be managed by spinal opioids.

Subarachnoid Versus Epidural Administration

Subarachnoid opioids have been used to control pain following a wide variety of surgical procedures and have the appeal of ease of administration, either at the time of spinal local anesthetic injection for surgical anesthesia, or as a separate technique when general anesthesia is administered. Because most clinicians give a single injection, this technique is best applied when surgical pain is expected to be of relatively short duration. Many patients remain comfortable for 24 hours or more after a single injection of subarachnoid morphine. Some of these patients will require no additional pain relief during their postoperative course or will find their remaining pain easily managed by oral analgesics. With the recent availability of small-gauge continuous spinal catheters, techniques for reinjection or infusion of subarachnoid narcotics are expected to evolve.

The epidural route has been used much more extensively for postoperative pain control. Reasons include popularity of the technique alone or in combination with light general anesthesia during surgery, willingness to leave an epidural catheter in place for extended periods to maintain analgesia, familiarity with postoperative analgesia using local anesthetics, and freedom from the risk of postlumbar puncture headache. Caudal epidural opioids have also been used effectively.[2]

Intraspinal Opioids Versus Patient-Controlled Analgesia

It is well known that certain surgical procedures result in more pain than others. Incisions involving the upper abdomen or thorax are expected to cause more pain than operations on the hand or foot. The postoperative pain therapist should be aware of the growing evidence that although patient-controlled analgesia (PCA) produces analgesia that is frequently superior to intramuscular opioids given on an as-needed basis, it may not produce as much pain relief as epidural opioid analgesia. Two studies report this finding in women following cesarean section,[8, 9] while the same observation has been made after open knee surgery[12] and cholecystectomy.[15]

Suprasegmental reflex responses to pain result in a stress response characterized by increased sympathetic tone, hypothalamic stimulation, increased catecholamine and catabolic hormone secretion (cortisol, adrenocorticotropic hormone, antidiuretic hormone, growth hormone, cAMP, glucagon, aldosterone, renin, angiotensin II), and decreased secretion of anabolic hormones (insulin, testosterone). The effects of these changes include sodium and water retention and increased blood glucose, free fatty acids, ketone bodies, and lactate. Metabolism and oxygen consumption are increased. Metabolic substrates are mobilized from storage depots. A catabolic state and negative nitrogen balance result if the process continues. The stress response after abdominal surgery is partially attenuated by IOA but not by systemic opioids.[10] Although it has not been determined whether attenuation of the stress response results in improved clinical outcome, it is logical to speculate that it might at least benefit certain patients, such as those with severe hypertension or advanced coronary artery disease.

For some patients, the additional analgesia available with IOA may be of critical importance. This is particularly true when severe pain compromises pulmonary function, leading to atelectasis and pneumonia. Examples include patients with rib fractures or pain resulting from abdominal and thoracic incisions. Those patients with underlying medical conditions such as respiratory insufficiency or obesity may also derive particular benefit from the best available analgesia. In these situations, the need for profound analgesia is of major importance and may make IOA the preferred choice.

Other factors may favor the selection of PCA for analgesia. Its use does not require the extra time and skill that is necessary for the anesthesiologist to place epidural catheters. The question of who will reinject epidural catheters day and night does not apply. The time required to educate ward nurses is less for PCA than for IOA. In some patient populations side effects such as nausea, pruritus, and urinary retention are more common and more severe with IOA than with PCA.

Certain clinical issues in patient selection remain controversial. What approach for postoperative pain control should be recommended in patients with opioid tolerance and/or drug-seeking behavior? IOA is frequently not successful in patients who demonstrate major opioid tolerance, although the combination of dilute local anesthetics and opioids (discussed later) infused through an epidural catheter has been more effective. Concern has been expressed that drug-seeking patients after surgery might abuse the opportunity to self-medicate with a PCA pump containing an opioid. Although the management of this population is never easy, we have found it useful after surgery to provide for such patients' basic preoperative opioid requirements with long-acting oral agents or fixed dose intravenous opioid infusions, while allowing them to use supplemental opioids from a PCA pump as needed for their incisional pain. Careful preoperative discussion ensures a clear understanding of the reason for each component of therapy including its planned duration. Conflict and anger postoperatively when it is time to remove the PCA pump are thus reduced. Even during optimal management, reported pain scores in this population are typically high, although objective observations show adequate respiratory patterns, effective coughing, and the ability to tolerate early ambulation and physical therapy.

Another area of controversy involves the management of postoperative pain in patients with coagulopathies or in those receiving anticoagulants to facilitate vascular or cardiac surgery. IOA may be of great benefit to some of these patients, but is it safe? There is no clear scientific answer. Each patient should be considered individually, with careful weighing of possible risks and expected benefits. Some anesthesiologists currently offer epidural anesthesia and analgesia to selected patients in this category; others do not. The interested reader is referred to a review of this subject.[20] PCA offers an attractive alternative in those situations when it is deemed prudent to avoid an epidural catheter.

TECHNICAL CONSIDERATIONS

Initiating Postoperative Intraspinal Opioid Analgesia

In patients receiving regional anesthesia for surgery, it is particularly easy to offer intraspinal opioids for postoperative pain. For example, a single dose of morphine may be added to the local anesthetic solution chosen for subarachnoid injection before transurethral prostatectomy. Similarly, an opioid may be injected repeatedly or infused continuously into a catheter that was placed in the epidural space to provide anesthesia for patients undergoing a wide variety of surgical procedures (e.g., cholecystectomy, hysterectomy, hip replacement, thoracotomy).

If general anesthesia was used for surgery, an epidural catheter can be placed any time in the postoperative period should pain control by other methods prove inadequate. Because correct placement of the catheter in the epidural space is essential for postoperative analgesia, neural blockade with a local anesthetic should be demonstrated before opioid injection. An adhesive transparent dressing over the catheter insertion site facilitates daily inspection. To minimize the risk of accidental epidural injection of drugs intended for intravenous administration,[11] we place a brightly colored intermittent injection cap (Product IN1000, Burron Medical, Inc., Bethlehem, PA) on the epidural catheter connector and a brightly colored label that reads "EPIDURAL CATHETER" on the catheter near the injection cap. Micropore filters are used on intrathecal and epidural catheters by some practitioners. They may reduce the risk of contamination by pathogenic organisms and prevent injection of foreign material such as glass particles. However, unlike chronically implanted catheters,[7] infections have not proved to be a problem in the postoperative period when filters are not used. Aspiration of epidural catheters to check for intravenous or subarachnoid migration is made difficult with some of these devices. A filtered needle used to draw up drugs from ampoules prevents injection of glass particles and represents a reasonable compromise.

The initial epidural opioid dose should given in the operating room at least 1 hour before the expected completion of surgery. It appears to be easier to establish good pain control immediately after surgery than to treat severe pain once it is established.[4]

Standard orders (Appendix A) governing care while IOA is used are recommended. These should include a notation of the initial opioid dose, an order for subsequent doses, monitoring instructions, orders for the treatment of common side effects, and definition of a physician to call if necessary. Our ward nurses have been provided with extensive inservice training to permit them to safely inject opioids into epidural catheters. Our standard orders provide for a fixed narcotic dose with a variable injection interval (e.g., preservative-free morphine, 4 mg every 6–12 hours). This gives the nurse some discretion in determining how frequently the dose will be administered. Standard orders should be tailored to the patient population, nursing practices, and medical preferences found in each institution.

Choice of Opioids

Table 1 lists a number of opioids, suggested dose ranges, expected latency, and duration of analgesia. Doses necessary to produce analgesia and their duration of effect vary considerably from one patient to another depending on age, medical condition, site of injection, type of pain, and other factors. Incorporating some of these factors, Table 2 lists suggested starting doses of epidural morphine, the most widely used opioid for incisional pain. The recommended doses are only rough guidelines. A dynamic ongoing assessment of adequacy of pain relief

Table 1. INTRASPINAL OPIOIDS FOR THE TREATMENT OF POSTOPERATIVE PAIN

Drug	Single Dose* (mg)	Infusion Rate† (mg/h)	Onset (min)	Duration of Single Dose‡ (h)
Epidural				
Morphine	1–6	0.1–1.5	30	6–24
Meperidine	20–100	5–20	5	2–6
Methadone	1–10	0.3–0.5	10	6–10
Hydromorphone	1–2	0.1–0.2	15	10–16
Diamorphine	4–6	?	5	12
Fentanyl	0.025–0.10	0.025–0.10	5	2–4
Sufentanil	0.01–0.06	0.01–0.05	5	2–4
Alfentanil	0.5–1	0.2	15	1–3
Subarachnoid				
Morphine	0.1–0.3		15	8–24+
Meperidine	10–30		?	10–24+
Diamorphine	1–2		?	20
Fentanyl	0.005–0.025		5	3–6

*Low doses may be effective when administered to the elderly or when injected in the cervical or thoracic region.

†If combining with a local anesthetic, consider using 0.0625% bupivacaine.

‡Duration of analgesia varies widely; higher doses produce longer duration.

Table 2. INITIAL DOSE (MILLIGRAMS) OF EPIDURAL MORPHINE FOR POSTOPERATIVE PAIN*

Patient Age (yr)	Nonthoracic Surgery (Lumbar or Caudal Catheter)	Thoracic Surgery	
		Thoracic Catheter	Lumbar Catheter
15–44	4	4	5
45–65	3	3	4
66–75	2	2	3
76+	1	1	2

These doses should only be considered as guidelines. Safe and effective doses for individual patients may vary considerably.

*These doses are based on the use of undiluted 0.1% preservative-free morphine.

for a particular patient with changes in dose and frequency of injection as necessary is the logical approach. Preservative-free morphine preparations have been used in a wide range of concentrations, with no apparent difference in efficacy. There is no reason to dilute the commercially available 0.1% solution. The addition of epinephrine to morphine is not recommended. Although most experience with morphine has involved intermittent injection, it has been used with success as a continuous infusion. Effective doses in our experience have ranged from less than 0.1 to 1.5 mg/h.

Elderly patients may need remarkably small doses of epidural morphine. In reviewing our experience treating women after abdominal hysterectomy, we found a significant negative correlation between age and effective dose of epidural morphine needed per 24 hours to achieve analgesia.[25] The relationship can be expressed by the following equation: effective 24-hour dose (mg) $= 18 - \text{age}\ (0.15)$.

A lipophilic agent such as fentanyl can be useful when rapid onset of analgesia is important. Intermittent epidural boluses of 50 to 75 μg can be used to promptly achieve analgesia in the immediate postoperative period if the initial epidural morphine dose is not adequate. Used as the sole opioid, a 25 to 100 μg epidural bolus is followed by a continuous infusion of 25 to 100 μg/h with an accurately calibrated pump. The predominant site of analgesic action using such infusions (spinal versus systemic) is controversial.[14] Repeated bolus injections and continuous infusions of opioids each have advantages and disadvantages. These are summarized in Table 3.

Locations for Use of Intraspinal Opioid Analgesia and Monitoring Issues

Along with early enthusiasm for IOA came sobering case reports of severe, life-threatening respiratory depression. These reports justifiably have been an ongoing source of concern regarding the use of intraspinal opioids, particularly beyond the confines of the intensive care unit. It is important to recognize that a great deal has been learned since the techniques were first introduced. Contemporary practice now

Table 3. EPIDURAL OPIOID BOLUSES VERSUS CONTINUOUS INFUSIONS

	Bolus	Infusion
Advantages	1. Simple 2. No special equipment 3. Regular aspiration test 4. Less rapid tolerance	1. No "peaks and valleys" 2. System remains closed 3. Well suited to short-acting opioids or local anesthetic/ opioid mixtures 4. No manpower needed to inject (physicians or nurses)
Disadvantages	1. Manpower needed to inject (physicians or nurses) 2. Human errors (drug, dose) 3. System "opened" for each injection 4. "Peaks and valleys"? 5. Not suited to short-acting opioids or local anesthetic/ opioid mixtures	1. More complex 2. More expensive 3. Human errors (drug, dose, pump settings) 4. "Set-up" time (delays) 5. Equipment failure 6. No aspiration test 7. Drug accumulation 8. More rapid tolerance
When to choose	1. With long-acting opioids 2. When nurses inject catheters 3. Pumps not available	1. With short-acting opioids 2. With local anesthetic/opioid mixtures 3. When nurses do not inject catheters

typically includes the following features: (1) Smaller opioid doses are currently used, with even greater dose reductions based on advanced patient age and poor physical status. In retrospect, the amount of epidural opioids often used during the period of initial experience with the technique were overdoses in contemporary terms. (2) The importance of avoiding large parenteral opioid doses and large doses of other CNS depressants in patients who will receive epidural opioids is now recognized. Such a combination increases the risk of respiratory depression. (3) The pattern of the respiratory depression that is most likely to occur is now better understood, in particular the fact that it is slow and progressive in nature rather than a sudden "out of the blue" apneic event. Short periods of apnea are common in patients receiving opioids by any route, or simply during sleep.[32] Such observations frequently are not clinically relevant and should not be taken as evidence that epidural morphine is dangerous. Under most circumstances there is no need to monitor for apnea.

It has been recognized that respiratory rate alone is not an adequate indicator of ventilatory status in all postoperative patients receiving intraspinal opioids.[24, 28] A more global assessment is necessary, particularly during the first 24 hours of treatment.[22] The utility of assessment of level of consciousness is now recognized. Increasing sedation (presumably due to a combination of central drug effect and CO_2 narcosis) has been noted with increasing respiratory depression.[27, 31] Healthy volunteers breathing CO_2 mixtures have been observed to lose consciousness at $P\text{co}_2$ levels of about 80 mm Hg.[29] Simple serial bedside assessment of level of consciousness (Table 4) is an excellent monitoring strategy and can be accomplished on any hospital ward without requiring additional nursing time.

Intensive care facilities are well suited to meet the needs of postoperative patients at special risk (advanced age, serious underlying conditions, extensive surgery). Does the use of an intraspinal opioid in a healthy patient make admission to the intensive care unit necessary? The expense and limited availability of these facilities makes this an impractical decision. Therefore, to require admission to the intensive care unit for the administration of epidural opioids is to deprive a large number of patients of the benefits of the technique. It is conceivable that some of these patients could die as a result of complications associated with inadequate analgesia (e.g., pneumonia, deep vein thrombosis, pulmonary embolus, myocardial infarction). It has now been demonstrated in a large number of both university and private institutions that postoperative intraspinal opioids can safely be offered on conventional hospital wards. Should intraspinal opioids be used on surgical floors in every hospital? The answer is clearly no. Guidelines for safe practice must be followed if such care is to be offered. These guidelines apply within or outside the intensive care unit[26]:

1. Careful patient selection with modification of opioid doses for patient age and physical status.
2. Regular follow-up by skilled and knowledgeable physicians.
3. Sound education of all nursing personnel regarding use and risks of intraspinal opioids, including instruction in bedside monitoring techniques that ensure early detection of respiratory depression.
4. Provision of periodic nursing education updates.
5. The use of printed protocols and standard orders developed jointly by physicians and nurses to govern the use of intraspinal opioids, including those permitting immediate intervention by nurses, if necessary.
6. Provision of a support system within the hospital that is capable of providing immediate airway management and ventilatory support at all times.
7. Continuing quality assurance review of all problems.

Using these guidelines, it can be argued that intraspinal opioids are as safe as intramuscular opioids administered anywhere in the hospital.

Table 4. EXAMPLE OF A BEDSIDE SEDATION SCALE

Sedation	Description
0 (none)	Patient alert
1 (mild)	Occasionally drowsy; easily aroused
2 (moderate)	Frequently drowsy; easily aroused
3 (severe)	Somnolent; difficult to arouse
S (sleep)	Normal sleep; easily aroused

Contraindications

Under some circumstances, spinal opioids are best avoided. These include (1) inexperience in performing lumbar puncture or epidural block, particularly in the cervical or thoracic regions; (2) known opioid allergies; (3) infection at the site of needle insertion; and (4) inadequate nursing education or monitoring capabilities.

Complications and Their Treatment

Respiratory Depression

Early respiratory depression occurring in the first 2 hours following injection is a feature of epidural opioid administration and is a result of vascular uptake and redistribution (i.e., the same mechanism that follows intramuscular injection). Delayed respiratory depression occurring between 6 and 12 hours following spinal or epidural injection is likely the consequence of rostral spread of the opioid in CSF. The target site is thought to be the respiratory center located superficially in the floor of the fourth ventricle. The actual incidence of this event is not known and is dependent on a number of factors, including the population studied, how they are monitored, and the definition of respiratory depression. In a questionnaire survey of 74 American institutions, the incidence of "respiratory insufficiency" was 1.9% to 2.3%.[18] In a large, multi-institutional Swedish questionnaire survey, the incidence was 0.09%.[22] In a prospective study involving 1085 patients in a single institution, the incidence of respiratory depression was 0.9%.[31]

It is not known whether the risk of severe respiratory depression is greater after spinal opioids than following opioid administration by more conventional routes. It has been reported that 860 hospitalized patients receiving morphine orally or parenterally (intravenously, intramuscularly, subcutaneously) demonstrated a 0.9% incidence of "life-threatening respiratory depression."[17]

The risk of delayed respiratory depression after intraspinal opioids appears to be greatest early in the course of therapy. There are no reported cases of this complication occurring later than 24 hours after administration of the initial dose of drug. Consistently impressive among predisposing risk factors are advanced age, concomitant use of systemic opioids or other CNS depressants, and extensive surgery.

The immediate treatment of severe respiratory depression is support of ventilation. Equipment to deliver oxygen with positive pressure must be readily available, and personnel in the area must be familiar with its use. Naloxone, 0.1 to 0.4 mg intravenously, will usually restore adequate spontaneous ventilation, but repeated doses are sometimes necessary. This drug should be kept at the bedside.

Pruritus

This symptom is common but seldom bothersome. The incidence is particularly high in obstetric patients. Itching may be generalized or localized, with the face being the most common site. Pruritus is seen both with opioids containing preservatives and preservative-free preparations. Although probably not due to histamine release, antihistamines often provide symptomatic relief. Naloxone is consistently effective but may have to be administered frequently or infused. Nalbuphine, 2 to 5 mg intravenously, provides symptomatic relief in some patients.

Urinary Retention

The incidence of this problem has been higher in volunteers than in patients, and higher in men. Naloxone may help prevent or reverse urinary retention, but doses approaching those that antagonize analgesia may be needed. Some patients require bladder catheterization.

Nausea and Vomiting

These distressing symptoms are believed to be the result of rostral spread of narcotic in CSF to the vomiting center and the chemoreceptor trigger zone located superficially in the floor of the fourth ventricle. Relief is frequently possible with antiemetics, but these may also produce unwanted sedation or even contribute to the risk or respiratory depression.[5] Transdermal scopolamine patches applied to the mastoid area have been effective.[13] A continuous naloxone infusion is also usually effective and should be considered when nausea and vomiting do not resolve with other measures.

Sedation

When any patient receiving intraspinal opioids appears excessively sedated, hypercarbia should be suspected and, if present, treated. The possible contributing role of other drugs such as antiemetics and antihistamines should also be considered. Sedation produced by intraspinal opioids, rarely a significant problem with moderate drug doses, may be the result of spread of the drug in CSF to receptors in the thalamus, limbic system, or cortex. Pharmacologic treatment is seldom indicated but physostigmine, 1 mg intravenously, may be effective.[30]

Technical Problems with Epidural Catheters

A number of technical problems can be expected using epidural catheters in postoperative patients. At the University of Washington Medical Center these have included premature dislodgement, pain during opioid injection, obstruction, and migration into epidural veins and into the subarachnoid space.

EPIDURAL POLYPHARMACOLOGY

Although continuous infusions of local anesthetics in usual clinical concentrations produce effective analgesia, they may also produce undesirable effects including hypotension, sensory and motor block, nausea, and urinary retention. In an attempt to achieve postoperative analgesia free of side effects, combinations of very dilute local anesthetics and opioids infused continuously through an epidural catheter have been advocated. Nociceptive pathways may be interrupted at different sites with the two drugs, namely the nerve axon with the local anesthetic and the spinal opiate receptor with the opioid. Bupivacaine appears to be well suited to this application because dilute solutions produce minimal motor block.

Cullen et al[6] used a mixture of 0.1% bupivacaine plus 0.01% morphine infused at a rate of 3 to 4 mL/h and compared it with the same concentrations of bupivacaine or morphine infused alone. Pain scores in the morphine and combination group were superior to the bupivacaine group. The only significant difference in side effects was a higher incidence of pruritus in both groups that received morphine. Hypotension or difficulty with ambulation were not apparent in the groups receiving bupivacaine.

It remains unclear whether the combination of epidural opioids and local anesthetics are superior for certain patients. The author has used a combination of fentanyl, 0.0002% (2 μg/mL), plus 0.0625% bupivacaine infused at a rate of 8 to 20 mL/h with good effect in patients with a known tolerance to opioids and in patients whose pain was not adequately controlled with epidural opioids alone. In addition to the monitoring used for patients receiving only epidural opioids, regular measurement of pulse, blood pressure, and sensory and motor examination is recommended. A sample of standard orders for epidural local anesthetic/opioid mixtures is provided in Appendix B.

Clonidine, an α_2-agonist, when given epidurally alone,[16] or in combination with a local anesthetic,[19] has been demonstrated to have analgesic properties. Its future role in postoperative pain control remains to be defined.

There remains a great deal to be learned regarding the optimal choice or combination of analgesic techniques for postoperative pain. Most institutions currently have limited options. The present situation can be likened to the early days of anesthesiology when the available drugs were limited (e.g., diethyl ether, nitrous oxide, chloroform). These were well suited to some applications and less well suited to others. Anesthetic practice of necessity was a "one size fits all" enterprise, and results reflected that practice. Over time, additional drugs were introduced into anesthetic practice. Other inhalational agents were more potent and reduced certain side effects. Muscle relaxants and opioids produced selective effects, permitting better control of the various elements of a complete anesthetic. Now a routine general anesthetic is likely to involve complex polypharmacology. At present, postoperative pain management using IOA can be likened to those early days of anesthesiology. The techniques represent major advances in postoperative pain therapy and can be used in a large number of situations. However, no single technique is ideally suited to all of them. As experience grows, subpopulations of postoperative patients will be defined for whom these and other new approaches, used alone or in combination, will be superior.

ECONOMIC ISSUES

Postoperative analgesia has traditionally been provided in the form of intramuscular opioids ordered by surgeons and administered by ward nurses on a as-needed basis. This has been considered part of the overall hospital care and, except for the drugs and the supplies used to administer them, no charges were generated. To use IOA effectively and safely, additional medical manpower is necessary. Differences in surgical populations, nursing practices, and medical preferences make all institutions unique. Each requires careful planning of an IOA program designed to suit its needs and resources. Such programs under the direction of anesthesiologists have been described.[21, 27] Physicians undertaking this task must be familiar with the pharmacology of analgesics, the possibility of drug interactions in hospitalized patients, and the short- and long-term effects of drugs given intraoperatively. It can be argued that anesthesiologists best fit this description. For optimal results, patients must be seen and assessed at frequent intervals by such physicians committed to, and readily available for, that purpose.

Should anesthesiologists be financially compensated for the time and responsibility associated with developing new pain treatment programs and for managing patients using IOA? The answer to this question may depend on what is provided by particular anesthesiologists. If the professional service consists simply of signing an order sheet and leaving patients on "auto pilot" while primarily engaging in other revenue-generating activities (such as operating room cases), it is hard to justify an additional patient charge. Furthermore, optimal results using IOA are not possible with such an approach. In many hospitals, anesthesiologists have assumed full responsibility for pain relief in patients using IOA and have committed manpower to the activity. Patients are seen and assessed at regular intervals and changes made in their care as necessary. Medical support is available at all times, not just "between cases." This includes nights, weekends, and holidays. Such a commitment of manpower and expertise deserves reasonable compensation. This is now recognized by the American Society of Anesthesiologists and is beginning to be recognized by patients and health insurance carriers.

References

1. Behar M, Olshwang D, Magora F, et al: Epidural morphine in the treatment of pain. Lancet 1:527–529, 1979
2. Boskovski N, Lewinski A, Xuered J, et al: Caudal epidural morphine for postoperative pain relief. Anaesthesiology 35:67–68, 1980
3. Chadwick HS, Ready LB: Intrathecal and epidural morphine sulfate for postcesarean analgesia—A clinical comparison. Anesthesiology 68:925–929, 1988
4. Chambers WA, Sinclair CJ, Scott DB: Extradural morphine for pain after surgery. Br J Anaesth 53:921–925, 1981
5. Cohen SE, Rothblatt AJ, Albright GA: Early respiratory depression with epidural narcotic and intravenous droperidol. Anesthesiology 59:559–560, 1983
6. Cullen ML, Staren ED, El-Ganzouri A, et al: Continuous epidural infusion for analgesia after major abdominal operations: A randomized, prospective, double-blind study. Surgery 98:718–728, 1985
7. DuPen SL, Peterson DG, Williams A, et al: Infection during chronic epidural catheterization: Diagnosis and treatment. Anesthesiology 73:905–909, 1990
8. Eisenach JC, Grice SC, Dewan DM: Patient-controlled analgesia following cesarean section: A comparison with epidural and intramuscular narcotics. Anesthesiology 68:444–448, 1988
9. Harrison DM, Sinatra R, Morgese L, et al: Epidural narcotic and PCA for postcesarean section pain relief. Anesthesiology 68:454–457, 1988
10. Kehlet H: Pain relief and modification of the stress response. *In* Cousins MJ, Phillips GD (eds): Pain Relief and Modification of the Stress Response. New York, Churchill Livingstone, 1986, pp 49–75
11. Lin D, Becker K, Shapiro HM: Neurologic changes following epidural injection of potassium chloride and diazepam: A case report with laboratory correlations. Anesthesiology 65:210–212, 1986
12. Loper KA, Ready LB: Epidural morphine following anterior cruciate ligament repair: A comparison with patient-controlled intravenous morphine. Anesth Analg 68:350–352, 1989
13. Loper KA, Ready LB, Dorman HB, et al: Prophylactic transdermal scopolamine reduces nausea in postoperative patients receiving epidural morphine. Anesth Analg 68:144–146, 1989
14. Loper KA, Ready LB, Downey M, et al: Epidural and intravenous fentanyl are clinically equal following knee surgery. Anesth Analg 70:72–75, 1990
15. Loper KA, Ready LB, Nessly M, et al: Epidural morphine provides greater pain relief than patient-controlled intravenous morphine following cholecystectomy. Anesth Analg 69:826–828, 1989
16. Mendez R, Eisenach JC, Kashtan K: Epidural clonidine analgesia after cesarean section. Anesthesiology 73:848–852, 1990
17. Miller RR, Greenblatt DJ: Drug Effects in Hospitalized Patients. New York, John Wiley and Sons, 1976, pp 151–152
18. Mott JM, Eisele JH: A survey of monitoring practices following spinal opiate administration. Anesth Analg 65:S170, 1986
19. Nishikawa T, Dohi S: Clinical evaluation of clonidine added to lidocaine solution for epidural anesthesia. Anesthesiology 73:853–859, 1990
20. Owens EL, Kasten GW, Hessel EA: Spinal subarachnoid hematoma after lumbar puncture and heparinization: A case report, review of the literature, and discussion of anesthetic implications. Anesth Analg 65:1201–1207, 1986
21. Ramsey DH: Perioperative pain: Establishing an analgesia service. *In* Brown DL (eds): Problems in Anesthesia—Perioperative Analgesia. Philadelphia, Lippincott, 1988, pp 321–326
22. Rawal N, Arnér S, Gustafsson LL, et al: Present state of extradural and intrathecal opioid analgesia in Sweden: A nationwide follow-up survey. Br J Anaesth 59:791–799, 1987
23. Rawal N, Sjöstrand U, Christoffersson E, et al: Comparison of intramuscular and epidural morphine for postoperative analgesia in the grossly obese: Influence on postoperative ambulation and pulmonary function. Anesth Analg 63:583–592, 1984

24. Rawal N, Wattwil M: Respiratory depression after epidural morphine—An experimental and clinical study. Anesth Analg 63:8–14, 1984
25. Ready LB, Chadwick HS, Ross B: Age predicts effective epidural morphine dose after abdominal hysterectomy. Anesth Analg 66:1215–1218, 1987
26. Ready LB, Edwards WT: Postoperative care following intrathecal or epidural opioids II. Anesthesiology 72:213, 1989
27. Ready LB, Oden R, Chadwick HS, et al: Development of an anesthesiology-based postoperative pain management service. Anesthesiology 68:100–106, 1988
28. Ready LB, Wild LM: Organization of an acute pain service: Training and manpower. Anesth Clin North Am 7:229–239, 1989
29. Sechzer PH, Egbert LD, Linde HW, et al: Effects of CO_2 inhalation on arterial pressure, ECG and plasma catecholamines and 17-OH corticosteroids in normal man. J Appl Physiol 15:454–458, 1960
30. Shulman MS, Sandler A, Brebner J: The reversal of epidural morphine induced somnolence with physostigmine. Can Anaesth Soc J 31:678–680, 1984
31. Stenseth R, Sellevold O, Breivik H: Epidural morphine for postoperative pain: Experience with 1085 patients. Acta Anaesthesiol Scand 29:148–156, 1985
32. Turner K, Sandler AN, Vosu H, et al: Respiratory pattern in postcaesarean patients after epidural or intramuscular morphine. Anesth Analg 68:S296, 1989
33. Wang JK, Nauss LA, Thomas JE: Pain relief by intrathecally applied morphine in man. Anesthesiology 50:149–151, 1979
34. Yeager MP, Glass DD, Neff RK, et al: Epidural anesthesia and analgesia in high-risk surgical patients. Anesthesiology 66:729–736, 1987

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APPENDIX A

EPIDURAL NARCOTIC STANDARD ORDERS

1. Operating room dose: Drug ________________ mg _____ Time ____.
2. Drug for continuing epidural analgesia:
   A. PF morphine (1 mg/mL) _____ mg q 6–12 hours.
   B. Fentanyl (10 μg/mL normal saline) infuse _____ μg (_____ mL) per hour.
   C. Other: Drug ________________ Concentration _____ Dose _____ Interval _____.
3. Fentanyl, 50 μg (1.0 mL), into epidural catheter q 3 h prn for inadequate analgesia with prescribed dose above.
4. Maintain IV access (drip or heparin lock) for 24 hours after last dose of epidural narcotic.
5. Naloxone, 0.4 mg, at bedside.
6. No narcotics or other CNS depressants to be given except as ordered by the Acute Pain Service.
7. Monitoring:
   Respiratory rate and sedation scale q 1 h for first 24 hours. Then q 4 h.
8. Treatment of side effects:
   A. Call Acute Pain Service for sedation scale = 3.
   B. Call Acute Pain Service for RR < 8 per minute.
   C. Naloxone, 0.4 mg *IV stat,* for sedation scale = 3 *plus* RR < 8 per minute. Call Acute Pain Service.
   D. Metoclopramide, 10 mg IV q 6 h prn, for nausea/vomiting. In addition, if age < 60 years, TRANSDERMAL SCOPOLAMINE PATCH to either mastoid area. Change q 72 h prn.
   E. Diphenhydramine, 25 mg IV q 6 h prn, for severe itching.
   F. For urinary retention, "in and out" bladder catheter prn.
9. For inadequate analgesia or other problems related to epidural, call Acute Pain Service.
10. Triazolam, 0.125 mg qhs prn. MR × 1.

APPENDIX B

EPIDURAL LOCAL ANESTHETIC/ NARCOTIC INFUSIONS

1. Infusion begun at ____ hours.
2. Drug for continuing epidural analgesia:
   ☐ Bupivacaine, 1/16% (0.625 mg/mL normal saline).*plus*
   ☐ Fentanyl, 2 µg/mL normal saline *or*
   ☐ PF morphine, 0.1 mg/mL normal saline *or*
   ☐ Other: Local anesthetic ____ Concentration ____
   Narcotic ____ Concentration ____.
   Infuse at ____ mL/h.
3. Fentanyl, 50 µg (1.0 mL), into epidural catheter q 3 h prn for inadequate analgesia with prescribed dose above.
4. Place at bedside:
   A. Ephedrine, 25 mg/5 mL (i.e., 5 mg/mL).
   B. Naloxone, 0.4 mg/1mL.
5. Maintain IV access (drip or heparin lock with flushes).
6. No narcotics or other CNS depressants to be given except as ordered by the Acute Pain Service.
7. Monitoring:
   A. BP/Pulse (via automatic BP monitor) from start of infusion q 30 min × 3 h; then q 1 h.
   B. Respiratory rate and sedation scale q 1 h for first 24 h; then q 2 h.
   C. Sensory level and motor function q 2 h while awake.
   D. Postural BP/P prior to first ambulation.
8. PRN treatments:
   A. Naloxone, 0.4 mg *IV stat,* for sedation scale = 3 *plus* RR < 8 per minute. Call Acute Pain Service.
   B. Metoclopramide, 10 mg IV q 6 h prn, for nausea/vomiting. *In addition, if age < 60 years,* transdermal scopolamine patch to either mastoid area. Change q 72 h prn.
   C. Diphenhydramine, 25 mg IV q 6 h prn, for severe itching.
   D. For urinary retention, "in and out" bladder catheter prn.
   E. Triazolam, 0.125 mg qhs prn. MR × 1.

9. Notify Acute Pain Service for the following:
   - A. BP < ____ mm Hg and/or P < ____ /min.
   - B. RR < 8/min.
   - C. Sedation scale = 3.
   - D. Numbness above nipples and/or inability to bend knees.
   - E. Posture BP drop > 15 mm Hg and/or HR increase > 20/min.
   - F. Inadequate analgesia or other problems related to epidural.

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MANAGEMENT OF POSTDURAL PUNCTURE HEADACHE

Joseph M. Neal, MD

In August 1898, the German surgeon August Bier demonstrated the first use of spinal anesthesia for the relief of surgical pain. Bier not only positively altered the future of anesthesiology, but also presented its practitioners with one of their most vexing problems. For in volunteering himself as a subject, Bier suffered the first reported postdural puncture headache (PDPH) and even suggested low CSF pressure as the etiology of his own discomfort.

This article reviews the pathophysiology and clinical presentation of PDPH and the factors that contribute to its prevention. The efficacy of various methods currently used to treat PDPH is the primary focus.

PATHOPHYSIOLOGY

Following Bier's suggestion, MacRobert[69] in 1918 postulated that continuous leakage of spinal fluid through a dural puncture hole was responsible for PDPH. Kunkle et al[63] expanded this hypothesis in 1943 by proposing two mechanisms responsible for the headache. First, CSF leaking out of the subarachnoid space allows the brain and its supporting structures to sag, especially when the patient assumes an upright posture. This places traction on the anchoring intracranial vascular structures, which are pain sensitive. Pain is referred along the trigeminal nerve to the frontal areas and along the vagus, glossopharyngeal, and first three cranial nerves to the occiput and neck. Second, traction and low pressure cause reflex vasodilatation of these same pain-sensitive

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vessels.[63] The reader is referred to an excellent review of these mechanisms by Brownridge.[12]

Indirect evidence supports, but does not prove, the previous hypothesis. Low CSF pressure has been demonstrated in patients with PDPH.[109] Headache can be elicited in the upright subject on removal of 20 mL of CSF and then relieved by replacement of the same volume with saline.[63] Actual leakage of CSF into the epidural space via dural puncture holes has been visualized with myeloscopy[83] and at laminectomy.[11]

Naulty et al[75] recently proposed two distinct phases of PDPH. The first occurs in the initial 36 hours and is associated with a relatively mild postural headache of 24 to 36 hours' duration. The proposed etiology is receiving spinal anesthesia with glucose-containing solutions of either lidocaine or bupivacaine. The second phase occurs later, is associated with CSF loss through the dura, and is not influenced by drug selection.[75] These observations remain unconfirmed and have been challenged by Culling.[34]

CLINICAL PRESENTATION OF POSTDURAL PUNCTURE HEADACHE

The pathognomonic feature of PDPH is its relationship to posture, wherein the headache begins shortly after assuming an erect or semi-erect position and resolves quickly on resumption of the supine position. The site of pain may be frontal, occipital, or both. Associated symptoms are inconsistent, but commonly include neckache or stiffness (57%), backache (35%), or nausea (22%). Less commonly seen are shoulder pain, blurred vision, tinnitus or vomiting,[2] and auditory difficulties.[109] Abducens palsy has been reported and may last longer than the headache.[56] The severity of PDPH is increased by pressure on the carotids, and decreased by pressure on the jugular veins.[63]

Headache may present immediately after dural puncture, but usually occurs 24 to 72 hours later. Rarely, PDPH presents 5 days after the instigating procedure.[60] Seventy per cent of PDPHs are relieved spontaneously within 7 days, and 95% resolve within 6 weeks.[109]

In general, PDPH incidence is increased in younger age groups and is more common in women than men, especially during pregnancy.[109] Previous history of PDPH may increase the likelihood of another headache.[68] Psychogenic factors perhaps play a role, as demonstrated by Kaplan's study showing no statistical difference in the incidence of PDPH between patients receiving spinal punctures and those receiving "sham" punctures.[61] Daniels and Sallie,[36] in studying Kiribati native cultures, state that PDPH is brought on by suggestion, and urge practitioners not to tell patients to expect a headache—clearly the opposite approach of current medicolegal precedent.

Differential Diagnosis

Always consider PDPH a diagnosis of exclusion. Especially when the headache is atypical, one should search for alternative etiologies. Many postsurgical patients complain of nonpostural headache. Migraine or tension headache, meningitis, or intracranial events should be ruled out. Diagnoses that could have been mistaken for PDPH include hypothalamic tumor[4] and sequelae of wound infection or eclampsia.[21]

PREVENTION OF POSTDURAL PUNCTURE HEADACHE

In their series of 11,574 carefully selected patients undergoing subarachnoid block with either a 26-gauge Quincke or 22-gauge Greene needle, Moore and Bridenbaugh[71] reported the overall incidence of PDPH as 1.4%. Other series have noted the incidence to be much higher. Postdural puncture headache may occur in up to 37% of patients undergoing spinal anesthesia,[43] 85% of patients having unintentional dural puncture secondary to attempted epidural anesthesia,[12] 37% of patients having diagnostic lumbar punctures, and 76% of patients undergoing myelogram.[98] The following factors influence the incidence of PDPH. Advantageous manipulation aids in prevention.

Small Spinal Needle Diameter

Vandam and Dripps'[109] classic compilation of 10,098 spinal anesthetics clearly showed a decreasing incidence of PDPH associated with decreasing needle diameter. A randomized, double-blind study by Tourtellotte et al[106] demonstrated a threefold increase of PDPH with a 22-gauge versus a 26-gauge needle. Multiple studies confirm these findings,[39, 48, 53, 85, 103] some describing remarkable decreases in PDPH achieved by using spinal needles only one size smaller.[6, 95] As patients become older, needle size may be less important as a factor in PDPH.[87] Recently, a number of in vitro studies have emphasized the importance of small needle diameter in reducing the rate of transdural CSF leakage.[32, 40, 73, 89]

Greene[51] in 1950 described a "double needle technique" that used a 21-gauge introducer to facilitate the placement of a 26-gauge spinal needle. Variations on this theme include passing a 30-gauge needle through an epidurally placed Tuohy needle.[66] Increased technical difficulty is reported as a frequent occurrence with needles smaller than 26 gauge.[14, 35, 66] The smallest usable needle is 33 gauge, since fluid cannot be injected through a 34-gauge spinal needle.[46]

Spinal Needle Tip Design

Designing spinal needle tips in such a way as to minimize trauma to the dura may lower the incidence of PDPH. Standard sharp point spinal needles, such as the Quincke or diamond tip, cut dural tissue and possibly cause dural rents to persist. Alternatively, blunt or rounded-point needles (Greene, Whitacre, Sprotte) are repudiated to spread dural fibers gently, allowing them to cinch closed after the needle is withdrawn. In vitro experimental evidence confirms that a conical needle tip causes less transdural leak; as does a 30- to 40-degree oblique approach to the dura and smaller needle diameter.[32, 55, 89]

An expanding body of clinical evidence supports this theory. In 1923, Greene[52] ground a standard spinal needle into a "round, sharp, tapering point." Only two headaches occurred in his next 215 patients.[52] There were no PDPHs in Moore's[72] 218 patients tapped with a 26-gauge Greene needle, as compared with six headaches in 217 patients (2.8%) given spinal anesthesia with a 22-gauge Greene needle. Neal et al[76] found no difference in the incidence of PDPH in 366 patients randomly assigned to undergo spinal anesthesia with either a 26-gauge Quincke needle or the larger 22-gauge Greene needle. Postdural puncture headache with the pencil-point (20 or 22 gauge) Whitacre needle (hole on the side) ranges from 0.34% to 3.8%.[15, 54, 93] Most recently the 24-gauge Sprotte needle (a more elongated pencil-point with lateral hole) has been reported to cause a 0.02% incidence of PDPH after 7175 diagnostic and surgical lumbar punctures.[101] This remarkably low incidence has been confirmed as less than 1% by two smaller studies of cesarean section patients.[18, 96]

Spinal Needle Bevel Orientation

Labat[64] was first to suggest spinal needles be inserted in such a manner as to orient their bevel parallel to longitudinal dural fibers. Following this reasoning, Franksson and Gordh[45] in 1946 postulated that a spinal needle bevel inserted parallel to the midline of the back would spread dural fibers and minimize CSF leakage, whereas perpendicular insertion would enhance leakage by cutting fibers. Their experiment confirmed twice as many torn dural fibers by a perpendicular bevel insertion as by a parallel one.[45] Microscopic investigation of human dura demonstrates both concentrically and longitudinally directed fibers. This configuration will likely minimize the tendency of a dural hole to gape when made by a longitudinally directed needle bevel.[42] Clinically, two contemporary studies have confirmed decreased incidence of PDPH when inserting a spinal[70] or epidural[77] needle with the bevel parallel to longitudinal dural fibers. Culling et al[33] recently presented their findings challenging these beliefs and contend that needle bevel orientation is not an important factor in PDPH. Two recent in vitro studies have likewise questioned bevel orientation as a determinant of transdural fluid leakage.[32, 40]

Ambulation After Dural Puncture

In years past, patients undergoing lumbar puncture were ordered to bed for 24 hours, with the goal of preventing PDPH. As the use of outpatient spinal anesthesia increases, anesthesiologists have again become concerned that early ambulation influences the pathogenesis of PDPH. One alarming study cited a 37% incidence of PDPH in 51 men (average age, 38 years) who received outpatient spinal anesthesia with a 25-gauge needle.[43] Although their headache incidence was much lower, Mulroy et al[74] noted a fourfold increase (5.2% versus 1.2%) of PDPH in ambulatory spinal anesthesia patients as compared with inpatients. While these reports are worrisome, a number of controlled studies have demonstrated no significant difference in the incidence of PDPH between those patients placed at 4 to 24 hours of bed rest versus those who were granted immediate ambulation.[16, 25, 60, 105, 110] The conflicting nature of these reports and the lack of a large, well-controlled study analyzing PDPH in those receiving ambulatory spinal anesthesia make it extremely difficult to state recommendations concerning anesthetic choice for these patients.

TREATMENT OF POSTDURAL PUNCTURE HEADACHE

A variety of proposed treatments for PDPH include analgesics, nonsteroidal antiinflammatory drugs, steroids, tannic acid, abdominal binders, forced hydration, lying prone, and implantation of catgut to plug the dural hole. None of these have proved to be consistently beneficial. Bed rest, analgesics, and hydration constitute accepted conservative treatment. It is best to avoid excessive hydration, because it frequently requires the patient to resume the upright position to micturate[22] and has not been shown to be advantageous.[62] Most PDPHs resolve in less than 7 days. Because the absence of headache after 24 hours often defines successful PDPH treatment, some "cures" likely represent the natural attrition of symptoms over time.

Three commonly accepted treatments for PDPH are infusion of epidural saline, intravenous or oral caffeine, and epidural blood patch (EBP). Caffeine probably relieves headache by reversing reflex vasodilatation of cerebral vessels; whereas EBP or saline infusion either stops the transdural leak of CSF or reestablishes normal CSF pressure. Rarely, patients will require surgical closure of the dura.

Epidural Saline

An early, yet current, treatment of PDPH involves the bolus or infusion of saline into the epidural space. Though proponents claim it is effective in up to 90% of patients, a high relapse rate limits the technique. Furthermore, multiple bolus or continuous infusion is labor intensive.

In 1950, Rice and Dabbs[90] reasoned that by infusing preservative-free saline into the epidural space, the resultant pressure increase would "splint" the dura and stop transdural leak. Employing both caudal and lumbar epidural approaches, they used either indwelling catheter or single injection techniques to instill 20 to 30 mL of saline. Twenty-one of 22 patients sustained complete and immediate headache relief, but over half relapsed within 20 hours. When symptoms returned, patients were reinjected, with the average patient requiring a total of 82 mL of saline to alleviate PDPH.[90]

Simply increasing epidural pressure may not fully explain the efficacy of this technique. Usubiaga et al[108] injected 10 to 20 mL of saline into the lumbar epidural space and monitored both epidural and subarachnoid pressures. Whereas subarachnoid pressures increased to 85 cm of water, and epidural pressures peaked at 65 cm of water, these effects only lasted 3 to 10 minutes and are likely too transient to account for the relief of headache. Higher pressures correlated with rapid injection and higher volumes and were associated with nausea, dizziness, and tachypnea. In this study, 8 of 11 patients had permanent relief of PDPH following the injection of 10 to 20 mL of epidural saline.[108]

Other studies evaluating the value of epidural saline are conflicting. Crawford[31] reported 16 patients who had suffered inadvertent dural puncture with an 18-gauge Tuohy needle and who subsequently received 1000 to 1500 mL of crystalloid solution infused into their epidural space over 24 hours. Sixty-eight per cent did not develop PDPH.[31] Using an epidural bolus technique, Craft et al[28] reported a 12.5% incidence of PDPH in 16 patients treated prophylactically with 60 mL of saline, as compared with a 76.5% incidence in 17 patients who did not receive prophylaxis. Less encouraging results were reported in a randomized, concurrent study of 29 parturients. The treated patients received epidural saline by catheter on the evening of and morning following inadvertent dural puncture. There was no difference in the incidence of PDPH between the treated and untreated groups.[94]

Two studies directly compare epidural saline injection to EBP. Bart and Wheeler[8] randomized 43 patients with PDPH to receive either 30 mL of epidural saline or a 10-mL EBP. The saline bolus was only 60% effective, whereas EBP was 100% effective in treating PDPH caused by a 25-gauge needle puncture. For those patients who sustained a 17-gauge needle puncture, saline relieved none of the headaches, whereas the blood patch relieved 73%.[8] Trivedi et al[107] analyzed prevention of PDPH with either prophylactic saline patch or blood patch. Twenty of 30 patients treated with 40 to 60 mL of saline following inadvertent dural puncture developed PDPH, as compared with only 1 of 11 patients who received a 15-mL EBP.

Caffeine Therapy

The etiology of PDPH partially relates to low spinal fluid pressure causing reflex dilatation of cerebral vessels with resultant pain. Since its vasoconstrictor properties were widely used to treat vascular headaches, Holder in 1944[57] suggested caffeine as a treatment for the headache that follows dural puncture. Proponents of caffeine tout it as a safe and effective alternative to EBP. Side effects (dizziness, flushing) have been reported as absent or mild,[1, 17, 58] even in nursing mothers.[97]

In 1978, Sechzer and Abel[97] published a double-blind demand study of PDPH patients treated with intravenous caffeine sodium benzoate (CSB). Seventy per cent of these patients had no return of headache following injection of CSB, 0.5 g/2 mL. Of particular interest in their study was the observation that caffeine increases cerebral arteriolar resistance, decreases cerebral blood flow and volume, and decreases CSF pressure. These changes in intracranial vascular dynamics lead to diminution of tension and traction on the pain-sensitive structures surrounding the brain. The observation that caffeine further decreases CSF pressure led these investigators to suggest that low CSF pressure is not likely an important factor in the etiology of PDPH.[97] Dodd et al[41] confirmed decreased cerebral blood flow from caffeine. Using a 133-xenon washout technique, 500 mg intravenous CSB caused an average 22% reduction of cerebral blood flow in seven patients with PDPH. Headache was relieved, but returned in 48 hours in all patients.[41]

A number of authors, citing complications of EBP, have urged CSB as the first-line treatment of PDPH.[9, 59] Jarvis et al[58] reported an 80% success rate in the treatment of PDPH in 20 patients. Caffeine, 500 mg, was initially infused in well-hydrated patients, then repeated in 4 hours if there was no symptomatic improvement. Abboud et al[1] reported that the same dose relieved PDPH in 92% of 25 obstetric patients, with a 57% recurrence rate.

Camann and associates[13] recently evaluated oral caffeine for the treatment of PDPH. Forty postpartum patients participated in this double-blind, placebo-controlled trial. Visual analog pain score at 4 hours improved in 90% of patients given 300 mg oral CSB, as compared with 60% in the nontreated group. At 24 hours, 30% of the treated group experienced recurrence of pain; and the visual analog pain score was not different between the groups. Patients given CSB experienced minimal side effects.[13]

The caffeine content of common beverages is listed in Table 1.

Epidural Blood Patch

Despite a few criticisms, EBP remains the gold standard for treatment of PDPH. Epidural saline infusion is 0% to 88% successful in treating or preventing PDPH[8, 28]; and caffeine therapy is 70% to 80% successful.[13, 58] The body of evidence documenting efficacy of EBP is significantly larger than for the other two techniques, and suggests an average success rate of 90% to 99%.[3, 78] In addition, the technique is safe, simple, and time efficient.

Gormley[50] reported in 1960 that patients receiving "bloody taps"

Table 1. CAFFEINE CONTENT OF COMMON BEVERAGES

Beverage	Caffeine (mg/100 mL)
Coffee	
Instant	44
Percolated	73
Dripolated	97
Tea, bagged	
Black, 5-minute brew	33
Black, 1-minute brew	20
Carbonated beverage	
Coca-Cola	18
Tab	14
Pepsi Cola	12

Data from MS Batra, MD, personal communication, 1991.

during spinal anesthesia had a decreased incidence of PDPH. Hypothesizing that blood around the dura may prevent CSF loss, he treated and cured a PDPH patient by injecting 2 mL of blood into the epidural space. Soon afterward Gormley suffered PDPH, and being perhaps more generous with himself, was cured with a 3-mL injection of autologous blood.[50] Five years later, Ozdil and Powell[80] described a unique experiment in which they obtained 2.5 mL of autologous blood, allowed it to clot, and injected it while withdrawing a spinal needle from the subarachnoid space into the epidural space. None of their 100 patients thus treated developed PDPH, whereas 15 of 100 untreated control patients did.[80]

DiGiovanni and Dunbar[37] in 1970 described what would become a common technique for EBP. Patients with PDPH were hydrated with 500 to 1000 mL of Ringer's lactate. Ten milliliters of autologous blood were aseptically drawn and then injected into the epidural space. Patients were kept supine for 30 minutes. Using this technique, the authors successfully treated 41 of 45 patients, achieving immediate and permanent relief of symptoms. The remaining four patients had relief within 24 hours. Except for mild, transient backache, none of the patients had complications from EBP; and the authors concluded it was a safe, effective treatment for PDPH.[37] They further stated that failure to relieve PDPH with EBP was likely due either to improper identification of the epidural space or an error in diagnosis.[38]

A small double-blind controlled study involving 12 patients confirms the efficacy of EBP. Seebacher et al[98] injected an average of 15 mL of blood into six patients with PDPH, five of whom obtained complete symptomatic relief. No patients given a sham EBP had relief of their headache.[98] Although most reports describe EBP following resolution of epidural anesthesia, Smith and Brown[100] successfully performed an EBP for PDPH and then 2 hours later administered epidural anesthesia for lithotripsy.

Mechanism of Action

No definitive study explains the mechanism of action of EBP. A long-held assumption asserts that clotted blood covers the dural hole and prevents leakage of CSF. Carrie[17] recently challenged this theory, doubting that CSF is produced rapidly enough to account for the immediate headache relief provided by EBP. He suggests that the mechanism involves increased epidural and subarachnoid pressure secondary to injection of blood volume. Subarachnoid pressure remains at 70% of peak pressure 20 minutes following injection of epidural blood.[26]

DiGiovanni et al[38] investigated the deposition of blood injected into the epidural space of angora goats. While the dural tear was immediately tamponaded by gelatinous blood, the actual fibroblastic repair of the hole did not occur until 48 hours later. Rosenberg and Heavner[91] studied the in vitro effects of EBP in a canine model. They concluded that the efficacy of EBP was from forming an adherent, coagulated patch over the dural hole, and that a clot plug may form in the hole as blood is forced through it and into the subarachnoid space. This patch can withstand the spinal pressure changes normally associated with sitting.[91] Of additional interest is the discovery that blood clots four times faster in CSF, thus placing doubt on the theory that some EBPs fail because they are "washed off" by CSF.[24]

Ideal Volume of Epidural Blood Patch

Although early reports of EBP advocated injection of 2 to 3 mL of blood into the epidural space, most recent sources suggest an amount of at least 15 mL.[37, 104] Ravindran[88] reported only 80% success using 8 to 10 mL of blood. Conversely, Crawford[30] recommends infusing up to 20 mL of autologous blood, stopping when the patient complains of back or leg pain. Ninety-seven of 98 patients experienced complete relief of PDPH with this regimen.

Szeinfeld et al[103] used a radioisotope imaging technique to define objectively the ideal amount of blood for EBP. An average 14.8 mL of blood injected into the epidural space spreads an average of nine spinal segments. Cephalad spread averaged six segments, over a wide range from L1 to T5. Caudad spread usually stopped at the S1 or S2 segment. Since blood preferentially spreads cephalad, they recommend using a spinal interspace lower than the original puncture site. They concluded, based on ten patients, that 12 to 15 mL of blood was the ideal amount for EBP; and advised discontinuing injection when the patient complained of the slightest discomfort in the legs, back, or buttocks. By adhering to this protocol, no patients suffered from residual radicular pain after EBP,[103] a finding also noted by Coombs and Hooper.[26]

Prophylactic Epidural Blood Patch

There is no clear consensus on attempting to prevent PDPH by blood patching patients immediately after unintentional dural puncture.

Proponents reason that since 70% of patients with large-gauge dural holes are likely to develop PDPH, aggressive attempts to prevent this complication are justifiable. Critics cite a lack of well-controlled studies supporting the efficacy of EBP when performed within 24 hours of dural tap[67] and the small but present risks associated with EBP.[113]

DiGiovanni et al[37] described five patients who were given prophylactic EBP following unintentional dural puncture. After withdrawing the Tuohy needle into the epidural space, a catheter is threaded and local anesthetic given. At the end of the obstetric procedure, 10 mL of blood was placed into the epidural space. None of the five patients developed headache.[37] Over the ensuing 20 years, several reports involving small numbers of patients have described prophylactic EBPs with 10 to 20 mL of blood, usually through an epidural catheter placed for labor and delivery. From 0% to 21% of these patients eventually developed PDPH.[3, 19, 23, 60, 88, 107] Two studies have unfavorably compared prophylactic EBP with other therapies. Balagot et al[5] demonstrated that a 7-mL prophylactic EBP was not superior to 7 mL of saline in preventing PDPH, and neither was superior to no treatment at all. In an uncontrolled study involving 86 postpartum patients, Palahniuk and Cumming[81] instilled 5 to 10 mL of blood through an epidural catheter in 11 of the patients. The incidence of PDPH was 59% in the untreated group and 54% in the treated group.[81]

Critics of prophylactic EBP[30, 79] base their objections partially on evidence that blood patching is ineffective in the first 24 hours. Loeser et al[67] randomly divided 66 patients with PDPH undergoing EBP (10 mL of blood) into two groups: an immediate group (<24 hours) and a delayed group (>24 hours). Seventy-one per cent of EBPs in the immediate group failed, compared with 4% in the delayed group[67]; findings that may simply suggest that early PDPH results from a more severe dural leak.

The lack of a large controlled study leads to difficulty in confidently evaluating the efficacy of prophylactic EBP. For those clinicians who elect to use this technique, a review of the existing literature suggests it reasonable to inject at least 15 to 20 mL of blood (or until the patient complains of discomfort) through the epidural catheter.

Complications of Epidural Blood Patch

Epidural blood patch is remarkably safe, as demonstrated in multiple studies with over 100 subjects each.[2, 29, 38, 78, 104] Contraindications to EBP are septicemia, local infection of the back, or active neurologic disease.[79] Despite early concerns, blood injected into the epidural space has not been reported to cause arachnoiditis or chemical meningitis.[38] There are no reports of infectious meningitis after EBP, although this concern was recently voiced in the case of an HIV-positive patient who received autologous EBP.[44] Two case reports have documented severe back pain with radicular signs and symptoms that completely resolved in 5 to 14 days. Irritation or traction of a nerve root by the clot is possibly the mechanism explaining this phenomena.[27, 99] Successful epidural anesthesia has been performed at various times after EBP,[2, 100] but there are reports documenting inadequate epidural blockade 3 years following EBP.[86]

The most common complication of EBP is transient back pain during the first 72 hours, which occurs in 35% to 100% of patients.[29, 104, 110] Lower extremity pain occurs in 12% of patients after EBP.[104] Abouleish et al[2] noted a 5% incidence of mild, transient temperature elevation; and a less than 1% incidence of patients complaining of neck pain. Avoid rapidly injecting large volumes of either epidural saline or blood. Intraocular hemorrhage occurs after epidural injection of large volumes (120 mL) of saline.[20] Coombs and Hooper[26] warn that neck pain, dizziness, tinnitus, or back and leg pain may indicate increasing subarachnoid pressure secondary to rapid injection or excessive volume.

One should carefully avoid placement of EBP too soon after injection of local anesthetic into the epidural space. Leivers[65] reported total spinal anesthesia occurring 2 minutes after injection of 15 mL of blood into the epidural space. The patient had received a top-up dose of 150 mg of lidocaine 35 minutes earlier. He suggests that diffused lidocaine in the CSF was forced cephalad by increased subarachnoid pressure consequent to placement of epidural blood. Local anesthetic block should therefore be allowed to dissipate before EBP.[65]

UNUSUAL MANAGEMENTS OF POSTDURAL PUNCTURE HEADACHE

The overwhelming success of EBP not withstanding, some patients have required inventive treatment methods or surgical correction to eliminate PDPH. Baysinger et al[10] reported two patients with persistent headache despite repeated EBP with 10 mL of autologous blood. These patients were treated with epidural saline bolus (30–40 mL) followed by patient-controlled, continuous infusion of saline at 15 to 25 mL/h over a 24-hour period. Their headache resolved without sequelae of back pain, orbital pain, or retinal hemorrhage.[10] A similar approach was used in a patient with a 4-month history of PDPH. Following two unsuccessful blood patches, the patient received a 24-hour saline infusion epidurally, but the headache relapsed in 48 hours. Following institution of a second 16-hour saline infusion, a 10-mL EBP was administered and resulted in permanent cure of the PDPH.[102] Epidural blood patch has been successful in a patient who suffered PDPH for 19 months before definitive treatment.[112]

Barrios-Alarcon et al[7] published a preliminary report of 56 patients with PDPH who were treated with an average of 20 mL of dextran 40 infused into the epidural space over 120 seconds. The study is concerning in that relief of headache followed a variable time course from 15 minutes to 24 hours. There was no recurrence of headache in any patient. The authors assumed the high molecular weight of dextran delayed its absorption from the epidural space, thereby resulting in prolonged epidural space pressure.[7]

Brown and Jones[11] described surgical correction of a dural rent. Their patient had persistent PDPH for 5 months after myelography for back pain. They discovered an actively leaking dural hole at the time of laminectomy. Cushing clips closed the hole, and the patient had no further headache.[11]

Failure of PDPH to resolve after the first EBP may be due to improper identification of the epidural space. Therefore, it may be prudent to confirm needle or catheter placement in the epidural space by establishing a short-acting local anesthetic block before the subsequent injection of blood.

SPONTANEOUS LOW CEREBRAL SPINAL FLUID PRESSURE HEADACHE

Although most postural headaches are clearly related to iatrogenic puncture of the dura mater, this syndrome has also been reported following surgery, head trauma, nerve-sleeve tears, or spontaneous rupture of nerve root-sleeve cysts (Tarlov cyst). The syndrome is commonly referred to as spontaneous low CSF pressure headache, but is also known as Schaltenbrand's syndrome, spontaneous aliquorrhea, or primary intracranial hypotension. Radionucleotide scanning with technetium-labeled human serum albumin and myelography are useful in making the diagnosis and identifying the site of dural leak.[92] Both continuous epidural saline infusion[49] and autologous EBP have been reported as effective in the treatment of spontaneous low CSF pressure headache.[47, 92]

SUMMARY

Postdural puncture headache occurs when leakage of CSF through a dural hole lessens the cushioning effect of the brain, allowing it to sag within the intracranial vault. This situation leads to reflex vasodilatation of and traction on pain-sensitive cerebral vascular structures. The resultant postural headache usually occurs 24 to 72 hours after initial dural puncture and will often persist 5 to 7 days without treatment. The use of smaller spinal needles with tips designed to spread dural fibers will dramatically decrease the incidence of PDPH. Relief of PDPH can be achieved with either epidural saline, or more reliably with intravenous caffeine sodium benzoate therapy. The most immediate and efficacious treatment of PDPH is autologous EBP, a simple technique remarkably free of major permanent complications. The role of prophylactic EBP remains controversial.

REFERENCES

1. Abboud TK, Zhu J, Reyes A, et al: Efficacy of intravenous caffeine for post dural puncture headache [abstract]. Anesthesiology 73:A936, 1990
2. Abouleish E, de la Vega S, Blendinger I, et al: Long-term follow-up of epidural blood patch. Anesth Analg 54:459, 1975

3. Ackerman WE, Colclough GW: Prophylactic epidural blood patch: The controversy continues [letter]. Anesth Analg 66:913, 1987
4. Alfery DD, Marsh ML, Shapiro HM: Post-spinal headache or intracranial tumor after obstetric anesthesia. Anesthesiology 51:92, 1979
5. Balagot RC, Lee T, Liu C, et al: The prophylactic epidural blood patch [letter]. JAMA 228:1369, 1974
6. Barker P: Are obstetric spinal headaches avoidable? Anaesth Intens Care 18:553, 1990
7. Barrios-Alarcon J, Aldrete JA, Paragas-Tapia D, et al: Relief of post-lumbar puncture headache with epidural Dextran 40: A preliminary report. Reg Anesth 14:78, 1989
8. Bart AJ, Wheeler AS: Comparison of epidural saline placement and epidural blood placement in the treatment of post-lumbar-puncture headache. Anesthesiology 48:221, 1978
9. Baumgarten RK: Should caffeine become the first-line treatment for postdural puncture headache? [letter]. Anesth Analg 66:913, 1987
10. Baysinger CL, Menk EJ, Harte E, et al: The successful treatment of dural puncture headache after failed epidural blood patch. Anesth Analg 65:1242, 1986
11. Brown BA, Jones OW: Prolonged headache following spinal puncture: Response to surgical treatment. J Neurosurg 19:349, 1962
12. Brownridge P: The management of headache following accidental dural puncture in obstetric patients. Anaesth Intens Care 11:4, 1983
13. Camann WR, Murray RS, Mushlin PS, et al: Effects of oral caffeine on postdural puncture headache: A double-blind, placebo-controlled trial. Anesth Analg 70:181, 1990
14. Cann JE, Wycoff CC: Incidence of headache with use of 27 gauge spinal needle. Anesthesiology 11:294, 1950
15. Cappe BE: Prevention of postspinal headache with a 22-gauge pencil-point needle and adequate hydration. Anesth Analg 39:463, 1960
16. Carbaat PAT, van Crevel H: Lumbar puncture headache: Controlled study on the preventive effect of 24 hours' bed rest. Lancet 2:1133, 1981
17. Carrie LES: Epidural blood patch: Why the rapid response? [letter]. Anesth Analg 72:129, 1991
18. Cesarini M, Torrielli R, Lahaye F, et al: Sprotte needle for intrathecal anaesthesia for Caesarian section: Incidence of postdural puncture headache. Anaesthesia 45:656, 1990
19. Christensen FR, Lund J: Accidental dural puncture: Immediate or delayed blood patch. Br J Anaesth 55:89, 1983
20. Clark CJ, Whitwell J: Intraocular haemorrhage after epidural injection. Br Med J 1:1612, 1961
21. Cohen S, Luykx WM, Marx GF: Obstetric complication as cause of post-spinal-block postural headache: Report of two cases. Reg Anesth 7:131, 1982
22. Cohen SE: Epidural blood patch in outpatients: A simpler approach [letter]. Anesth Analg 64:546, 1985
23. Colonna-Romano P, Shapiro BE: Unintentional dural puncture and prophylactic epidural blood patch in obstetrics. Anesth Analg 69:522, 1989
24. Cook MA, Watkins-Pitchford JM: Epidural blood patch: A rapid coagulation response [letter]. Anesth Analg 70:567, 1990
25. Cook PT, Davies MJ, Beavis RE: Bed rest and postlumbar puncture headache. The effectiveness of 24 hours' recumbency in reducing the incidence of postlumbar puncture headache. Anaesthesia 44:389, 1989
26. Coombs DW, Hooper D: Subarachnoid pressure with epidural blood "patch." Reg Anesth 4:3, 1979
27. Cornwall RD, Dolan WM: Radicular back pain following lumbar epidural blood patch. Anesthesiology 43:692, 1973
28. Craft JB, Epstein BS, Coakley CS: Prophylaxis of dural-puncture headache with epidural saline. Anesth Analg 52:228, 1973
29. Crawford JS: Epidural blood patch [letter]. Anaesthesia 40:381, 1985
30. Crawford JS: Experiences with epidural blood patch. Anaesthesia 35:513, 1980
31. Crawford JS: The prevention of headache consequent upon dural puncture. Br J Anaesth 44:598, 1972
32. Cruickshank RH, Hopkinson JM: Flow through dural puncture sites. An in vitro comparison of needle point types. Anaesthesia 44:415, 1989

33. Culling RD, Rubin A, Culclasure J, et al: Spinal headaches: Bevel orientation not an important factor [abstract]. Reg Anesth 15:32, 1990
34. Culling RD: Local anesthetics and post-dural puncture headaches [letter]. Anesthesiology 73:587, 1990
35. Dahl JB, Schultz P, Anker-Moller E, et al: Spinal anaesthesia in young patients using a 29-gauge needle: Technical considerations and an elevation of postoperative complaints compared with general anesthesia. Br J Anaesth 64:178, 1990
36. Daniels AM, Sallie R: Headache, lumbar puncture, and expectation [letter]. Lancet 1:1003, 1981
37. DiGiovanni AJ, Dunbar BS: Epidural injections of autologous blood for postlumbar-puncture headache. Anesth Analg 49:268, 1970
38. DiGiovanni AJ, Galbert MW, Wahle WM: Epidural injection of autologous blood for postlumbar-puncture headache. II. Additional clinical experiments and laboratory investigation. Anesth Analg 51:226, 1972
39. Dittmann M, Renkl F: Spinal anesthesia with extremely fine needles [letter]. Anesthesiology 70:1035, 1989
40. Dittmann M, Schäfer HG, Ulrich J, et al: Anatomical re-evaluation of lumbar dura mater with respect to postspinal headache. Effect of dural puncture. Anaesthesia 43:635, 1988
41. Dodd JE, Efrid RC, Rauck RL: Cerebral blood flow changes with caffeine therapy for postdural headaches [abstract]. Anesthesiology 71:A679, 1989
42. Fink BR, Walker S: Orientation of fibers in human dorsal lumbar dura mater in relation to lumbar puncture. Anesth Analg 69:768, 1989
43. Flaatten H, Raeder J: Forum: Spinal anesthesia for outpatient surgery. Anaesthesia 40:1108, 1985
44. Frame WA, Lichtmann MW: Blood patch in the HIV-positive patient [letter]. Anesthesiology 73:1297, 1990
45. Franksson C, Gordh T: Headache after spinal anesthesia and a technique for lessoning its frequency. Acta Chir Scand 94:443, 1946
46. Frumin MJ: Spinal anesthesia using a 32-gauge needle. Anesthesiology 30:599, 1969
47. Gaukroger PB, Brownridge P: Epidural blood patch in the treatment of spontaneous low CSF pressure headache. Pain 29:119, 1987
48. Geurts JW, Haanschoten MC, van Wijk RM, et al: Post-dural puncture headache in young patients. Acta Anaesthesiol Scand 34:350, 1990
49. Gibson BE, Wedel DJ, Faust RJ, et al: Continuous epidural saline for the treatment of low CSF pressure headache. Anesthesiology 68:789, 1988
50. Gormley JB: Treatment of postspinal headache. Anesthesiology 21:565, 1960
51. Greene BA: A 26 gauge lumbar puncture needle: Its value in the prophylaxis of headache following spinal anesthesia for vaginal delivery. Anesthesiology 11:464, 1950
52. Greene HM: Lumbar puncture and the prevention of postpuncture headache. JAMA 86:391, 1926
53. Harris LM, Harmel MH: The comparative incidence of postlumbar headache following spinal anesthesia administered through 20 and 24 gauge needles. Anesthesiology 14:390, 1953
54. Hart JR, Whitacre RJ: Pencil-point needle in prevention of postspinal headache. JAMA 147:657, 1951
55. Hatfalvi BI: The dynamics of post-spinal headache. Headache 17:64, 1977
56. Heyman HJ, Salem MR, Klimov I: Persistent sixth cranial nerve paresis following blood patch for postdural puncture headache. Anesth Analg 61:948, 1982
57. Holder HG: Reactions after spinal anesthesia. JAMA 124:56, 1944
58. Jarvis AP, Greenawalt JW, Fagraeus L: Intravenous caffeine for post-dural puncture headache [abstract]. Reg Anesth 11:42, 1986
59. Jarvis AP, Greenawalt JW, Fagraeus L: Intravenous caffeine for postdural puncture headache [letter]. Anesth Analg 65:313, 1986
60. Jones RJ: The role of recumbency in the prevention and treatment of postspinal headache. Anesth Analg 53:788, 1974
61. Kaplan G: The psychogenic eiology of headache post lumbar puncture. Psychosom Med 29:376, 1967
62. Kaukinen S, Kaukinen L, Kannisto K, et al: The prevention of headache following spinal anaesthesia. Ann Chir Gynaecol 70:107, 1981

63. Kunkle EC, Ray BS, Wolff HG: Experimental studies on headache: Analysis of the headache associated with changes in intracranial pressure. Arch Neurol 49:323, 1943
64. Labat G: The trend of subarachnoid block. Surg Clin North Am 10:671, 1930
65. Leivers D: Total spinal anesthesia following early prophylactic epidural blood patch. Anesthesiology 73:1287, 1990
66. Lesser P, Bembridge M, Lyons G, et al: An evaluation of a 30-gauge needle for spinal anesthesia in Caesarean section. Anaesthesia 45:767, 1990
67. Loeser EA, Hill GE, Bennet GM, et al: Time vs. success rate for epidural blood patch. Anesthesiology 49:147, 1978
68. Lybecher H, Moller JT, May O, et al: Incidence and prediction of postdural puncture headache. A perspective study of 1021 spinal anesthesias. Anesth Analg 70:389, 1990
69. MacRobert RG: The cause of lumbar puncture headache. JAMA 70:1350, 1918
70. Mihic DN: Postspinal headache and relationship of needle bevel to longitudinal dural fibers. Reg Anesth 10:76, 1985
71. Moore DC, Bridenbaugh LD: Spinal (subarachnoid) block: A review of 11,574 cases. JAMA 195:907, 1966
72. Moore DC: Factors influencing spinal anesthesia. Reg Anesth 7:20, 1982
73. Morrison LMM, Haindl H, Sinclair WA, et al: In vitro comparison of CSF leakage after dural puncture with Haindl, Sprotte and Quincke needles [abstract]. Reg Anesth 15:14, 1991
74. Mulroy MF, Neal JM, Bridenbaugh LD, et al: Is post-spinal headache more frequent in outpatients? [abstract]. Reg Anesth 14(2S):2, 1989
75. Naulty JS, Hertwig L, Hunt CO, et al: Influence of local anesthetic solution on postdural puncture headache. Anesthesiology 72:450, 1990
76. Neal JM, Bridenbaugh LD, Mulroy MF, et al: Incidence of post dural puncture headache is similar between 22G Greene and 26G Quincke spinal needles [abstract]. Anesthesiology 71:A678, 1989
77. Norris MC, Leighton BL, DeSimone CA: Needle bevel direction and headache after inadvertent dural puncture. Anesthesiology 70:729, 1989
78. Ostheimer GW, Palahniuk RJ, Shnider SM: Epidural blood patch for post-lumbar-puncture headache [letter]. Anesthesiology 41:307, 1974
79. Ostheimer GW: Prophylactic epidural blood patch. Reg Anesth 4:17, 1979
80. Ozdil T, Powell WF: Post lumbar puncture headache: An effective method of prevention. Anesth Analg 44:542, 1965
81. Palahniuk RJ, Cumming M: Prophylactic blood patch does not prevent post lumbar puncture headache. Can Anaesth Soc J 26:132, 1979
82. Parris WCV: Use of epidural blood patch in treating chronic headache: Report of six cases. Can J Anaesth 34:403, 1987
83. Pool JL: Myeloscopy: Intraspinal endoscopy. Surgery 11:169, 1942
84. Quaynor H, Corbey M: Extradural blood patch—Why delay? Br J Anaesth 57:538, 1985
85. Quaynor H, Corbey M, Berg P: Spinal anesthesia in day-care surgery with a 26-gauge needle. Br J Anaesth 65:766, 1990
86. Rainbird A, Pfitzner J: Restricted spread of analgesia following epidural blood patch: Case report with a review of possible complications. Anaesthesia 38:481, 1983
87. Rasmussen BS, Blom L, Hansen P, et al: Postspinal headache in young and elderly patients: Two randomized, double-blind studies that compare 20- and 25-gauge needles. Anaesthesia 44:571, 1989
88. Ravindran RS: Epidural autologous blood patch on an outpatient basis [letter]. Anesth Analg 63:962, 1984
89. Ready LB, Cuplin S, Haschke RH, et al: Spinal needle determinants of rate of transdural fluid leak. Anesth Analg 69:457, 1989
90. Rice GG, Dabbs CH: The use of peridural and subarachnoid injections of saline solution in the treatment of severe postspinal headache. Anesthesiology 11:17, 1950
91. Rosenberg PH, Heavner JE: In vitro study of the effect of epidural blood patch on leakage through a dural puncture. Anesth Analg 64:501, 1985
92. Rupp SM, Wilson CB: Treatment of spontaneous cerebrospinal fluid leak with epidural blood patch. J Neurosurg 70:808, 1989

93. Sami HM, Skaredoff MN: In-hospital incidence of post-lumbar puncture headaches in Caesarean section patients associated with the 22 G Whitacre needle [abstract]. Reg Anesth 14:44, 1989
94. Santos DJ, Barrett T, Lachica R, et al: Efficacy of epidural saline patch in preventing post-dural puncture headache [abstract]. Reg Anesth 11:42, 1986
95. Sarma VJ, Bostrom U: Intrathecal anaesthesia for day-care surgery: A retrospective study of 160 cases using 25- and 26-gauge spinal needles. Anaesthesia 45:769, 1990
96. Sears DH, Leeman MI, O'Donnell RH, et al: Incidence of postdural puncture headache in Cesarean section patients using the 24G Sprotte needle [abstract]. Anesthesiology 73:A1003, 1990
97. Sechzer PH, Abel L: Post-spinal anesthesia headache treated with caffeine. Evaluation with demand method. Part I. Curr Ther Res 24:307, 1978
98. Seebacher J, Ribeiro V, LeGuillou JL, et al: Epidural blood patch in the treatment of post dural puncture headache: A double blind study. Headache 29:630, 1989
99. Shanta TR, McWhirter WR, Dunbar RW: Complications following epidural "blood patch" for postlumbar-puncture headache. Anesth Analg 52:67, 1973
100. Smith HS, Brown DL: Epidural anesthesia performed 2 hours after epidural blood patch. Reg Anesth 13:13, 1988
101. Sprotte G, Schedel R, Pajunk H, et al: Eine atraumatische Universalkanüle für einzeitige Regionalanaethesien. Regional-Anaethesie 10:104, 1987
102. Stevens RA, Jorgensen N: Successful treatment of dural puncture headache with epidural saline infusion after failure of epidural blood patch. Acta Anaesthesiol Scand 32:429, 1988
103. Szeinfeld M, Ihmeidan IH, Moser MM, et al: Epidural blood patch: Evaluation of the volume and spread of blood injected into the epidural space. Anesthesiology 64:820, 1986
104. Tarkkila PJ, Miralles JA, Palomaki EA: The subjective complications and efficiency of the epidural blood patch in the treatment of postdural puncture headache. Reg Anesth 14:247, 1989
105. Thornberry EA, Thomas TA: Posture and post-spinal headache: A controlled trial in 80 obstetric patients. Br J Anaesth 60:195, 1988
106. Tourtellotte WW, Henderson WG, Tucker RP, et al: A randomized, double-blind clinical trial comparing the 22 versus 26 gauge needle in the production of the post-lumbar puncture syndrome in normal individuals. Headache 12:73, 1972
107. Trivedi NS, Eddi D, Shevde K: Prevention of headache following inadvertent dural puncture [abstract]. Reg Anesth 14:51, 1989
108. Usubiaga JE, Usubiaga LE, Brea LM, et al: Effect of saline injections on epidural and subarachnoid pressures and relation to postspinal anesthesia headache. Anesth Analg 46:293, 1967
109. Vandam LD, Dripps RD: Long-term follow-up of patients who received 10,098 spinal anesthetics. JAMA 161:586, 1956
110. Vilming ST, Schrader H, Monstad I: Post-lumbar-puncture headache: The significance of body posture. Cephalalgia 8:75, 1988
111. Wetchler BV, Brace DE: A technique to minimize the occurrence of headache after lumbar puncture by use of small bore spinal needles. Anesthesiology 16:270, 1955
112. Wilton NCT, Globerson JH, de Rosayro AM: Epidural blood patch for postdural puncture headache: It's never too late. Anesth Analg 65:895, 1986
113. Woodworth GE: Prophylactic epidural blood patch in obstetrics [letter]. Anesth Analg 70:568, 1990

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LUMBAR AND CERVICAL EPIDURAL STEROID THERAPY

J. David Haddox, DDS, MD

The use of lumbar and cervical epidural steroid therapy is a longstanding practice. Although typically done by anesthesiologists, other practitioners, such as orthopedic surgeons and neurosurgeons, employ the technique as well. No data exist on the number of epidural steroid injections done annually in the United States, but common wisdom would lead one to believe that this is a rather frequent procedure. People who do the technique, of course, believe that it provides a benefit to their patients. This line of therapy has ardent supporters and detractors. Neither have the benefit of rigorous scientific validation of their opinions.

The literature involving epidural steroid therapy is largely retrospective or anecdotal. Numerous studies have been done; however, clear-cut irrefutable conclusions from this literature are not forthcoming. Often the study has a transparent bias, which may be either for or against the technique. Few studies clearly define their populations, but rather use diagnostic terms that imply the assumption that all practitioners will agree on what constitutes a given diagnosis, such as cervical radiculopathy. Some of the often quoted studies are confusing when read critically, especially in terms of the number of subjects that actually underwent or benefited from specific interventions.

In reviewing papers for this article, an effort was made to concentrate on those that met commonly accepted research design criteria, such as being randomized, prospective, placebo controlled, and blinded. In some cases, notably those studies involving cervical epidural

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steroid therapy, papers meeting these criteria were not available. Nevertheless, an effort has been made to distill this literature to look for valid inferences that can be made and to point the direction for further investigation.

HISTORY

Two papers involving this therapy are reviewed for their historical interest. The first, by Norman Viner, was published in 1925.[37] It was a series of three case reports, although the tone of the article implied a much larger experience with the technique. Viner used a caudal approach to treat sciatica. The mixture injected included 20 mL of 1% procaine, which was followed by the injection of 50 to 100 mL of Ringer's solution, normal saline, or liquid petrolatum. Three or four of these injections were given at 1-week intervals. He stated that the "more clear-cut the sciatica, the more effective was the treatment, and where it was combined with other factors, as for example lumbo-sacral pain, the latter was relatively little affected." He postulated that a counterirritation mechanism was the most acceptable explanation for benefit. He observed the three patients for varying amounts of time and reported them to be nearly symptom free at the end of the follow-up.

In 1930 William Evans published a series of 40 cases of unilateral sciatica that were treated by caudal injections.[16] In his introductory paragraphs, he stated that "The nomenclature adopted in the definition of the varied forms of sciatica is in a state of chaos." The modern literature, as is shown, still suffers from this problem.

He used a follow-up period that ranged from 1 to 42 months, with 17 patients being followed for over 1 year, and an additional 12 being followed for over 3 months. He reported 22 patients as "cured," by which he meant that they had experienced immediate relief from the pain and had remained symptom free, with resumption of their occupation and lifestyle. Two of these patients required two injections, the remainder benefited from only one treatment. Five cases were classified "improved" in that they reported significant reduction in their sciatic pain but occasionally experienced slight pain after the treatments. In nine cases there was a temporary improvement followed by return of pain (seven) or no relief from the procedure. Four patients were lost to follow-up. From cadaver investigations he theorized that a mechanical stretching of the nerve routes forming the sciatic nerve appeared to be important in modulating benefit. He did not explain this in any significant detail.

He noted that six of the "cures" had received injections of normal saline alone. He took this as adding credence to the concept of mechanical stretching mediating pain relief.

It is interesting to note that it was not until 1934 that Mixter and Barr[24] published their often quoted paper describing intervertebral disk herniation as a cause of sciatica.

Numerous other studies have been done since, with new ideas as to the mechanism of action of epidural steroids (to be discussed) and larger numbers of patients. However, many of these suffer from the same limitations as these earlier studies, namely inadequate clarification of pathologic diagnosis, lack of a standard treatment protocol, no blinding, and no controlling for placebo effects or for the natural history of low back pain.

LUMBAR EPIDURAL STEROIDS

Any discussion of epidural therapy must take into account the research that has been reported on using epidural local anesthetics alone. One of the best known papers involving a comparison between epidural local anesthetics and bed rest in treating sciatica was published by Coomes in 1961.[9] Coomes studied 40 patients with sciatica who had failed simple analgesic therapy. All patients had been symptomatic for about 1 month before the study. Careful analysis of history and physical examination excluded patients who were likely to be symptomatic for some other cause. Fifty milliliters of 0.5% procaine was injected caudally in 20 patients. After the injections they were allowed to return home and were not given any special advice. The patients were followed up to 9 weeks. Numerous parameters were assessed. At the end of treatment 12 of the epidural group had improved neurologic findings compared with five of the bed rest group. Two of the bed rest group were worse, while none of the epidural group had deteriorated. The remainder in each group were unchanged. The time to recovery, on average, was 31 days for the bed rest group compared with 11 days for the epidural group.

Recovery was defined as being relieved of pain when "up and about," with a normal straight leg raising test. Coomes refuted the mechanical hypothesis of Evans, stating he had injected similar amounts of normal saline on three occasions in comparable patients with no improvements whatsoever. He believed a hydrostatic effect in combination with anesthetizing the nerve sheath was contributing to the benefit.

Swerdlow and Sayle-Creer[35] published a large series in 1970. The initial group consisted of 530 patients complaining of backache, who were considered to be suffering from "the lumbo-sciatic syndrome." These patients were treated over a 10-year period with either normal saline, local anesthetic, or methylprednisolone acetate. In the early years of their study local anesthetic and normal saline were given by either the caudal or lumbar route. In the later years of their study methylprednisolone was given exclusively by the lumbar route. Three hundred twenty-five patients had been followed for at least 12 months, and they comprised the data base for this paper.

For the purpose of reporting, the patients were divided into three categories: an acute group, who were experiencing their first episode of pain, a chronic group in whom pain had existed for some time, and a recurrent group, who had had intervals of freedom from pain punctuated by attacks of pain. All the patients in this latter group were experiencing pain at the beginning of the study. They also classified their results into three groups. Relief was classified as necessitating no other treatment for that particular episode of lumbosciatic pain. They used the term "assisted" when there was sufficient temporary improvement to allow other forms of treatment to ensue. The remaining patients were considered to have had no value from the treatment.

When analyzing their data they found no difference between results produced by saline and local anesthetic alone. Therefore, they combined these data in their analysis into one treatment arm and compared this against methylprednisolone in each of the three categories of patients. In the acute group, no difference was seen between the use of local anesthetic or saline and methylprednisolone. Approximately one third of this group found either treatment to be of no value. In the recurrent group 46% were relieved or assisted by the local anesthetic or saline, whereas 61% received some benefit from the methylprednisolone treatment. In the chronic group, however, 45% of the steroid-treated patients were "relieved" compared with 27% of the local anesthetic/saline–treated group. When combining relieved and assisted patients, 67% of the methylprednisolone-treated patients benefited compared with 41% of the local analgesic/saline–treated patients. This was a statistically significant difference. The authors postulated that the effect of methylprednisolone was to reduce irritation or inflammation of affected nerve roots and reduce edema. The authors concluded that "in selected cases of lumbo-sciatic pain extradural medication will shorten the time of recovery from severe pain, avoid hospitalization or long periods of bed rest and allow earlier physiotherapy."

The first prospective randomized trial comparing a local anesthetic to a local anesthetic plus steroid was performed by Beliveau[3] and published in 1971. He used a study group of 48 consecutive patients who were thought to have moderate-to-severe unilateral sciatica caused by an intervertebral disk lesion. Patients were admitted without regard to presence or absence of neurologic findings and without regard to experience with conservative treatments. Clinical examination, radiographs of the lumbar spine and sacroiliac joints, and erythrocyte sedimentation rate were performed on all patients to rule out any rheumatologic condition.

They employed 42 mL of 0.5% procaine or 40 mL of 0.5% procaine plus 2 mL of methylprednisolone by the caudal route. Patient activity after the injections was not restricted. One week after the injection they classified patients into four groups: completely relieved, improved, unchanged, or worse. Repeat injections were offered to those in the "improved" group. In all, 82 injections were performed in the 48 patients. Follow-up ranged from 1 to 3 months after the first injection.

Summarizing their results, the authors observed that the injection of procaine alone was of benefit in patients who had had severe symptoms of a short (under 1 month) duration or in patients who had

had a long duration of moderate severity. The local anesthetic plus steroid provided substantial benefit in all instances, including long duration of severe symptoms. However, when looking at the raw data, one is at a loss to discern any difference between the treatments, although 70% of those treated with either injection improved, whereas 30% of the entire group were unchanged or worse. In this reasonably well-conceived study, no clear-cut differences were apparent by the addition of a steroid in the caudal epidural space.

Dilke et al[14] published the first prospective randomized double-blind study of epidural steroid injections. Their study initially involved 100 consecutive patients; however, their results were reported on somewhat fewer patients. Admission criteria were the presence of pain in the sciatic or femoral distribution, accompanied by painful sciatic or femoral stretch, sciatic scoliosis, or appropriate neurologic deficits. Any patients not thought to have diskogenic pain, or who had bilateral manifestations or previous surgery to the spine, or in whom there was any doubt of the technical success of the injection were excluded from the study.

The treatment group received 80 mg of methylprednisolone in 10 mL of normal saline given epidurally in the lumbar region. The control group received an injection of 1 mL of normal saline into the interspinous ligament. Local anesthetic infiltration of the skin was performed in all groups. All injections were performed by the same individual and neither the patient nor the clinician or his staff knew which type of injection had been received by a particular patient. Nonsteroidal anti-inflammatory drugs were used routinely, as was diazepam in a dose of 2 mg by mouth three times per day. In addition to the injection therapy, all patients underwent a graded program of exercise and other physical therapy interventions. A second injection was given at the end of 1 week if the clinician in charge believed that it was warranted. Numerous parameters were monitored.

At the conclusion of the study, there was no significant difference in the time of full bed rest, the time to instituting spinal flexibility exercises, or the time spent in the hospital. However, at 3 months follow-up, 33 of 36 patients in the treatment group had returned to work compared with 14 of 35 in the control group. This was significant at $P = 0.01$. During the hospital admission, 16 of the treatment group stated that their pain had been "clearly relieved" compared with four of the control group. This was also significant. At 3 months, seven patients in the treatment group used analgesics daily while 19 used none, compared with 14 and 11 in the control group, respectively. The authors concluded that epidural steroid appeared to offer some benefit over a placebo injection in terms of disability and pain. This was despite no significant difference in the groups in regard to neurologic deficits and nerve stretch tests. This group also thought that the anti-inflammatory effect of the steroid was the operant factor. They noted that the time course of improvement after the injection was gradual, taking from 1 to 4 days before maximum benefit ensued.

Another prospective randomized controlled study was performed by Breivik et al.[5] These results were published in 1976. The study involved 35 patients with incapacitating chronic pain in the low back and sciatica, who had been unresponsive to conservative treatment for several months to several years before the study. Eleven patients had undergone previous surgery for herniated nucleus pulposus removal. The authors injected either 20 mL of 0.25% bupivacaine, with 80 mg of methylprednisolone, or 20 mg of 0.25% bupivacaine followed by 100 mL of saline. If no improvement was seen 3 weeks after an injection, up to three injections of the alternative solution were administered. Physical therapy and other medical treatment was uniform. Both the patients and the evaluating neurologist were blind to the treatment given. Considerable relief was defined as a significant decrease in pain or weakness to the point that a patient could return to work or could engage in vocational rehabilitation.

In the bupivacaine/steroid group, 9 of 16 patients had considerable pain relief. Six of these had objective neurologic improvement. This is compared with 5 of 19 patients receiving bupivacaine/saline who reported considerable relief with objective neurologic change. Combining all possible injections, 25% improved after bupivacaine/saline and 63% improved after bupivacaine/methylprednisolone. This was a statistically significant difference. The authors believed that because 25% of their patients had improved with the bupivacaine/saline treatment, this should be offered as an initial option, to be followed by bupivacaine/steroid if no relief resulted from the former injection. They postulated that the steroid worked via an anti-inflammatory effect, whereas the saline and local anesthetic may work through breaking a pain-spasm-ischemia-pain cycle or placebo effect.

In 1978 Yates[42] published a series involving 20 patients and 49 injections. Four epidural injectates were available, all given by the caudal route: 50 mL of saline, 50 mL of 0.5% lidocaine, 47 mL of saline plus 3 mL of triamcinolone hexacetonide, or 47 mL of 0.5% lidocaine plus 3 mL of triamcinolone hexacetonide. The study was of a prospective, randomized type. The injections were give 1 week apart, with assessment of symptom severity immediately before and 30 minutes after each injection. Patients were given up to four injections (one of each injectate) as long as their symptoms persisted. Patients in whom symptom resolution occurred before the fourth injection were removed from the trial. In addition to subjective measurements of pain decrease, lumbar spine range of motion and straight leg raising tests were also evaluated. There was a tight correlation between the objective and subjective criteria.

Using the lumbar spine range of motion as a sole criterion, significant differences were seen between the saline/steroid and saline groups. When straight leg raising was used as the criterion, significant differences appeared between the saline/steroid and saline groups and the lidocaine/steroid and lidocaine groups, and the saline/steroid and lidocaine groups.

This study allowed each patient to act as their own control. No significant effort was made to control for any particular diagnosis.

Despite the lack of homogenous diagnoses and separate treatment of control groups, the results indicated that the steroid-containing solutions provided the greatest benefit. The authors recommended triamcinolone be used for epidural injections because it had the longest duration of action of steroids that were commonly available.

Cuckler et al[10] performed a randomized prospective double-blind placebo-controlled study of epidural steroids in the treatment of lumbar radiculopathy. This is a relatively recent paper (1985) and deserves special comment because, at first glance, its design appears to be one of the most rigorous in the literature. The authors studied 73 patients who had a clinical diagnosis of either lumbar radiculopathy or spinal stenosis. All patients had failed at least 2 weeks of conservative therapy that included bed rest and non-steroidal anti-inflammatory drugs. Patients with a previous surgical history were admitted only if their symptoms were clearly different from their initial symptoms and there had been at least a 6-month symptom-free period after the initial back surgery. Further inclusion criteria included positive findings on myelography, computed tomography, or epidural venography that were consistent with the patients' complaints and clinical findings.

A total of 7 mL of epidural injectate was placed via the L3-4 interspace with the patient in the lateral decubitus position, with the painful side down. Each 7 mL contained 5 mL of 1% procaine plus one of two combinations: 2 mL of saline or 2 mL of sterile water containing methylprednisolone, 80 mg. At 24 hours postinjection an attending physician and a resident evaluated each patient. Those who reported less than 50% pain relief received a second injection of procaine and methylprednisolone. The second injection was not blinded and was given 24 hours after the first.

Results were defined as follows: short-term success was equated to at least 75% improvement at 24 hours and long-term success was defined as at least 75% improvement at a period of observation between 13 to 30 months after the injection, with a mean follow-up of 20.85 months. Follow-up was done by the attending physician during routine office visits. Pain was the only parameter evaluated.

Sixty-one percent of the patients who received an epidural steroid injection as their first injection reported some degree of improvement, while 62% of the 32 patients who received placebo first reported some degree of improvement. The mean percentage estimate of improvement for the group was around 42%, with no difference in this figure between the steroid or placebo group. Short-term (24 hour) results demonstrated that 7 of 22 patients with the diagnosis of herniated nucleus pulposus benefited from steroid injection, while 5 of 14 benefited from placebo injection. In the spinal stenosis group, 5 of 20 benefited from steroid at 24 hours and 3 of 17 benefited from placebo. These were not significant differences. Long-term results found success in six of the steroid-treated group with a diagnosis of herniated nucleus pulposus and five with a diagnosis of spinal stenosis. Two in each diagnostic category were considered long-term successes after receiving placebo injections. These were not considered statistically significant. The authors concluded that "until large-scale randomized–blind studies can be performed, the use of epidurally administered steroid preparations must be regarded as one of the many unproved modalities that are used in treating lumbar radiculopathy."

The study appears to have several flaws in its design, despite a great deal of attention to this aspect of the paper. All epidural injections were given at the same interspace, regardless of the level of pathology. This certainly goes against common wisdom and would directly conflict with the study by Winnie et al,[41] which demonstrated that the level of the steroid placement was critical to success. Evaluating patients for success or failure on a short-term basis at 24 hours flies in the face of numerous studies that have indicated that a period of several days is typically required before benefit secondary to steroid is seen. Likewise, the patients were not offered subsequent injections, with the exception of after 24 hours, and numerous papers would suggest that if partial relief is obtained, improved benefit may accrue when subsequent injections are given at several-week intervals. Despite these flaws, which this author believes represent an obvious bias, the paper does serve as a model for attention to study design, which is not characteristic of this literature.

A different approach was taken by Davis and Emmons[12] in a study published in 1990, which compared the effects of direct instillation of methylprednisolone onto exposed nerve roots during unilateral lumbar laminotomies for disk excision at L4 or L5. Thirty-five of these patients were having their first back surgery. The results were compared with the results of matched control groups in whom the exact same procedures were done without the instillation of steroid intraoperatively. The authors evaluated the length of hospital stay, the need for strong analgesics, the need for mild analgesics, and need for drugs to help control muscle spasm. In all of these areas, the treated group had significantly lower values. For example, the hospital stay for first time laminotomy patients receiving methylprednisolone averaged 2.6 days compared with 4.11 days in the control groups. The decision to discharge was based on when patients were able to comfortably ambulate free of pain and spasm. The same trend held true in the repeat laminotomy group. Although this study does not relate specifically to what anesthesiologists think of as epidural steroids, it does lend credence to the notion that the steroid itself is beneficial and that placing the steroid at the level of the lesion is useful.

An interesting paper by Abram and Hopwood,[1] published in 1991, looked at the factors that contribute to successful outcome with lumbar epidural steroids. Two-hundred twelve patients were studied. All patients were thought to have at least some component of radiculopathy, and this was the primary diagnosis in 77% of the patients. An extensive pain questionnaire was completed by each patient before treatment. All patients were treated by placement of 50 mg of triamcinolone diacetate in 3 to 5 mL of 1% lidocaine. Repeat injections were based on partial improvement and were done up to a total of three over a 6-week period. Excellent response and no response were reasons for patients not getting repeat injections. After completion of treatment, a global reading of success was made by the pain medicine physician.

Patients with a longer duration of symptoms had a lower success rate. Patients whose pain was less than 6 months in duration had a 69.1% success rate, while those with pain of 6 months to 3 years had a 47.8% success rate, and those with pain over 3 years had a 40.6% success rate. Pretreatment pain rating had no bearing on success rate. Patients who are out of work because of their pain or who had frequent sleep disruption were less likely to respond to epidural steroids. Sixty-three percent of the patients diagnosed with radiculopathy as the main diagnosis responded, while only 23% of those with other primary diagnoses responded.

Approximately half of the patients returned 6-month follow-up questionnaires. Patients initially categorized as successful were still thought to be successes 62% of the time. Ratings of pain reduction and incidence of employment at 6 months follow-up were significantly better for patients who were initially considered successful. The majority of patients in both group decreased their pain medication use in the 6 months following their treatment. These 6-month trends persisted in that group of patients who responded to a 12-month follow-up questionnaire.

In summary, it appears that epidural steroids, while not a panacea, do appear to generally offer some benefit to patients with various back pains. Radicular type pains appear to respond better. It remains inconclusive at this juncture as to what benefit is conferred by the use of local anesthetic as a diluent as opposed to normal saline. Although many authors interpret a single saline injection that is followed by a beneficial response as a placebo effect, the duration of benefit demonstrated by some studies would make placebo response a less likely explanation and would argue for some other effect of the saline injection.

CERVICAL EPIDURAL STEROIDS

The literature regarding cervical epidural steroids contains far fewer studies than does the literature concerning lumbar epidural steroid placement. The difference in numbers of papers may reflect clinical experience with the two techniques, although one author has reported on a series of 790 injections.

In 1986 Purkis[27] published data on 113 cervical epidural injections that were provided to 58 patients. All of the patients had had pain for at least 6 months from a variety of conditions. Many had tried other interventions that were unsuccessful. The diagnoses were as follows: degenerative joint disease/osteoarthritis (16), chronic cervical sprain/flexion–extension injury (17), occipital neuralgia (17), and postherpetic neuralgia (8).

Patients were given a maximum of three injections at 2- to 3-week intervals based on degree of improvement from the preceding injection. An average of 1.95 injections were given per patient. All patients were assessed at 3 weeks after the last injection. Beyond that, no long-term follow-up was carried out in a systematic fashion; however, patients were instructed to return to the facility if symptoms should recur. A percentage change in preinjection and postinjection visual analogue scores was computed. This was fractionated into categories of no change, 20% decrease, 20% to 50% decrease, 51% to 75% decrease, 75% to 95% decrease, and pain free. All injections were done at the C5-6 level and a catheter was used if the level of pathology was suspected to be higher. Following a test dose of 1 mL of 1.5% lidocaine, 120 mg of methylprednisolone or triamcinolone was injected along with 2 mL of 1.5% lidocaine.

Of the 16 patients with degenerative joint disease, ten reported a greater than 50% decrease in their pain, with two reporting 100% pain relief at 3 weeks. The average number of injections per patient was 1.75. The group with chronic cervical sprain contained 12 patients out of the 17 with that diagnosis who reported greater than 50% pain relief, with an average injection rate of 1.81. The occipital neuralgia group, which contained 17 patients, also had 12 patients report greater than 50% pain relief at 3 weeks follow-up, but required an average of 2.53 injections per patient. The postherpetic neuralgia group, containing eight patients, who had pain in the cervical dermatomes, had four patients who reported greater than 50% pain relief, although only one reported complete relief and the other three were in the 51% to 75% category. These patients required, on average, 2.75 injections.

Overall, the study by Purkis reported that 38 of the 58 subjects (65.5%) had greater than 50% relief of their symptoms at 3 weeks, with 9 of the 58 stating that they were totally pain free at that interval. Twenty-two of their patients returned to the facility for the next 2.5 years, with the majority of them returning between 3 and 6 months following the last injection. Three patients had significant relief for more than 1 year, and one patient (diagnostic category not specified) was "virtually pain free" for 2.5 years following the last injection. Their complications were few and are reviewed later in the chapter.

Rowlingson and Kirschenbaum[30] published a retrospective study of 45 cervical epidural steroid injections performed on 25 patients with a diagnosis of cervical radiculopathy. Unlike many papers in this literature, these authors go into substantial detail about what constitutes the diagnosis for their study group. They required a history of radicular pain extending from the neck into the arm (two patients reported pain radiating from the neck only as far as the shoulder), neurologic changes on physical examination, or laboratory study results that were consistent with or suggestive of cervical radiculopathy (electromyelography, myelogram, CT scan, or plane radiographs). Most patients underwent electromyography; however, the other diagnostic studies were performed, on average, in under half of the study group. They injected 50 mg of triamcinolone diacetate mixed with 2 mL of 1% lidocaine for a total volume of 4 mL per injection. All injections were done at the

C6-7 or C7-T1 interspace. No catheters were employed. Repeat blocks were performed based on substantial but incomplete improvement and were done at 2-week intervals to a total of three injections. The mean injection rate per patient was 1.8. They categorized their responses as excellent (complete resolution of symptoms), good (> 75% improvement in symptoms with full return to previous life style), fair (mild improvement in the patient's condition), and poor (little or no change). The average follow-up for the entire group was about 6 months, with better responders being followed for a shorter amount of time, presumably due to patient preference (i.e., patients who were doing well felt little need to return to the facility).

Six of the 25 patients studied (24%) achieved excellent responses, with an average of 1.5 injections per patient. Forty percent of the group had good responses, with an average of 1.8 injections, while six patients reported a fair response, with an average of two injections per patient. Three patients reported poor responses, despite having positive histories consistent with radicular pain and abnormal physical examination or laboratory studies.

The authors thought that the technique was accepted by the patients without any difficulty. They emphasized that cervical epidural steroid injection was, in itself, insufficient to ensure "ultimate therapeutic response" and state that other treatments should be ongoing. Their patients were taking nonsteroidal anti-inflammatory drugs and were participating in physical therapy on a daily basis during the study. They also comment on the importance of the patient attitude in the rehabilitation process.

Shulman[34] reported a series of 96 patients who had undergone cervical epidural steroid injections for chronic neck pain between 1977 and 1983. He performed the injections at the C5-6 or C6-7 level using the loss-of-resistance technique. Methylprednisolone, in doses varying between 80 and 160 mg, was administered with either 1% lidocaine (2.5–20 mL) or 0.5% bupivacaine (4–15 mL). Muscular trigger points that were contributing to the complaints in the shoulder or neck area were also injected with bupivacaine. None of their patients had undergone cervical spine surgery.

Their diagnoses ranged from spondylosis (66) to radiculopathy (21), with nine patients having other miscellaneous diagnoses. Seventy-five percent of their patients received one injection while 21% received two injections. The remainder had three or more. Follow-up consisted of a telephone interview at an unspecified time after the injections were completed. The author used a rating system similar to that used by Purkis, as described previously. Forty-one percent of the patients reported good to complete pain relief, while 35% reported fair and 24% reported poor relief. Comparing the duration of relief with the degree of relief, Shulman state that 28 of the 39 patients reporting good to complete relief also reported the relief to have lasted for at least 1 month. In the fair to poor category, 86% of the patients reported relief for less than 1 month.

A series of 16 patients treated with epidural steroid injection for complaints of severe intractable pain in the neck and arm associated with numbness in an appropriate radicular distribution was reported by Warfield et al.[40] The patients had all failed numerous trials of conservative therapy and nonsteroidal anti-inflammatory drugs. The pain complaints had been present for at least 3 months before the study. Eighty milligrams of methylprednisolone was injected along with 5 mL of normal saline into the epidural space at the C6-7 or C7-T1 levels. The protocol for repeating the blocks entailed at least a 2-week interval between injections, with a total of three injections in a 6-month period. Repeat examination was performed 1 to 2 weeks after the last injection, and long-term follow-up was obtained by mail and telephone up to 1 year after the last injection.

One patient reported elimination of pain that lasted for 1 year. Three others reported improvement that persisted at least 1 year, while four patients reported improvement lasting at least 5 months at the time of publication. In all, 12 patients reported benefit. Six of these had improvement in neurologic findings during the study. Six patients who required analgesics before the procedure were able to decrease their analgesic use by 62.5%. Of the various factors analyzed, a decreased range of motion was the only one to correlate significantly with a good response to epidural injection. Like the study by Rowlingson and Kirschenbaum,[30] Warfield et al did not find electromyography results to correlate well with the likelihood of response to epidural steroid injections.

Cicala et al,[7] reported their results at 6-month follow-up of 79 patients who had received cervical epidural steroid injections. At 6 months, 58 patients were able to be evaluated. Their study population included diagnostic categories of spondylosis (25), strain (16), and other diagnoses, i.e., bulging disk, postlaminectomy syndrome, and "nonspecific radiculopathy" (17 total). All but one injection were performed at the C7-T1 interspace, using a loss of resistance technique. One half percent lidocaine (10–15 mL) was injected, along with 1 mg/kg of methylprednisolone acetate. Some injections were repeated; however, the number was not specified. The initial follow-up was at 24 and 72 hours using a "verbal analogue percentage scale," with the same instrument being used to evaluate the patients again at 6 months. The results were classified as follows: an excellent result meant greater than 90% pain relief lasting for the full 6-month follow-up, a good result meant greater than 50% pain relief lasting for at least 6 weeks, while a poor result was less than 50% pain relief or any degree of pain relief lasting less than 6 weeks.

Fifty-three of the 58 patients had pain relief immediately after the injection, while 49 noted relief at 72 hours. Fifty-six percent of the spondylosis group reported excellent pain relief at follow-up and 24% reported their pain relief to be good. Fifty-six percent of the group with "strain" reported excellent relief at 6 months, while 44% reported poor relief. In the miscellaneous group, only one patient reported excellent relief, with 11 reporting good relief, and five reporting poor relief. Overall, 41.4% of the patients receiving cervical epidural steroids reported excellent relief at 6 months, with an equal proportion reporting either good or poor results. The authors caution about the effect of the natural history of some of these conditions positively influencing their results, but do not state any figures to indicate how long the patients in their study had been symptomatic before receiving the injection.

In summary, it appears that cervical epidural steroids do offer the potential for some benefit in patients suffering from radiculopathy and cervical strain syndromes. However, no blinded control randomized studies currently exist that irrefutably support this contention.

EPIDURAL STEROIDS COMBINED WITH OPIATES

A review of this type of therapy would not be complete without reference to the reports of combining epidural steroids with epidural morphine for the treatment of low back pain. In 1986, Cohn et al[8] reported a series of epidural injections of both morphine and methylprednisolone in 20 patients with postoperative recurrent low back pain. All patients had failed conservative therapies and were without opiates or CNS depressants for at least 3 days before beginning the study. An epidural catheter was placed above the presumed site of insult and 8 mg of preservative-free morphine was injected through the catheter, followed 1 hour later by 80 mg of methylprednisolone acetate. The patients were then monitored for 24 hours.

Within 30 minutes, morphine had provided some degree of pain relief for all patients. This, however, was not without its cost in that 80% of the patients experienced pruritus, 40% were nauseous, 45% vomited, 25% were somnolent, and 20% had urinary retention. The mean age of this group was 48.55 years, with 14 of them over the age of 40.

At 24 months follow-up, seven patients continued to report 100% pain relief. At 6 months follow-up this figure had been 12 patients. Seventy percent pain relief was reported by five patients at 6 months, four patients at 12 months, and three patients at 24 months. Therefore, 10 of the original 20 patients reported 70% to 100% pain relief at 24 months follow-up.

These outstanding clinical results spurred two other papers in the next few years.

Dallas et al[11] reported on 20 patients treated in a manner similar to the patients of Cohn et al, except they used a double-blind saline controlled crossover design. They had rather mixed diagnostic categories, as did Cohn et al, but all of their patients were postlaminectomy.

They combined the data from the two groups and looked at the number of patients who reported greater than 50% pain relief with each technique (morphine plus steroid versus saline plus steroid). Sixty-five percent of the patients had greater than 50% relief for at least 24 hours with either or both of the study injectates. When morphine plus steroid was compared with saline plus steroid, the former resulted in a longer duration of relief. The maximum duration of relief, however, was 6 weeks. The peak time for a patient to report relief was at 2 weeks, prompting the authors to suggest that perhaps a repeat injection at 2 weeks would be beneficial. They further suggested that morphine combined with steroid might be beneficial in patients who appear resistant to the effects of epidural steroids alone.

In 1989 Rocco et al[29] did a double-blind study of postlaminectomy patients who were randomized to receive 1 mL of 5% lidocaine with 1.9 mL of triamcinolone diacetate or 8 mg of preservative-free morphine or both. These were done at 1-month intervals for 3 consecutive months. Medication was given at the level thought to be responsible for the patient's complaint. Twenty-two patients were followed. To analyze their results they looked at short-term pain relief (1–29 days), long-term relief (30 days or greater), and side effects.

No difference in short-term relief was evident among the different injectates. When pain relief did occur, it lasted 1 to 3 days except in one patient who had 2 weeks of relief on one occasion. One patient in the triamcinolone group experienced pain relief that lasted longer than 1 month.

The respiratory rates in the morphine group, as might be expected, were less than those in the triamcinolone group. The combination of the two drugs, however, resulted in a lower mean respiratory rate than the morphine group. Additionally, there was a longer time for return of the respiratory rate to baseline in the group that received both drugs. In 5 of 19 incidences, the combination group required naloxone for reversal of respiratory depression. Three of seven patients who received both drugs were responsible for all instances of respiratory depression requiring naloxone treatment. All of these had respiratory rates less than 12 with $PaCO_2$ values of 44 mm Hg or above, and PaO_2 values of 73 or less.

The authors concluded that none of their patients, which seems to be comparable to the patients in the two other studies, obtained long-term pain relief from this technique. In addition, they reported life-threatening ventilatory depression. They postulate that by injecting the steroid and the morphine simultaneously that the depot vehicle of the steroid may have retarded the vascular absorption of the morphine and, thereby, enhanced its dural penetration, causing greater toxicity. The final conclusion was that epidural morphine combined with a depot steroid was neither effective nor safe in the treatment of postlaminectomy pain syndrome.

MECHANISM OF ACTION OF EPIDURAL STEROIDS

Why should epidural steroids be effective for the treatment of low back pain? Several theories have been offered over a number of years and some of the theories have been reviewed in the earlier portion of this article. Surgeons who operate on patients with radiculopathy will state that the nerve root that is causing the problem is easily identifiable by its edematous inflammatory character. In 1988 Takata et al[36] demonstrated swelling in the nerve roots of the cauda equina in 16 of 28 patients who had myelographically proven herniated nucleus pulposus and who complained of sciatic pain. The CT technology they employed was target reconstruction, which allowed them to schematically represent the dorsal and ventral roots at the affected levels. They used a grading system to represent the amount of swelling. Grade 0 signified that the diameters of the affected ventral and dorsal roots were identical to those of the unaffected root diameters. Grade 1 indicated that they were less than twice the diameter of the unaffected side, while grade 2 indicated that they were more than twice the diameter on the nonsymptomatic side. Nine patients were classified as having grade 1 swelling and seven patients had grade 2 enlargement. All patients who had a swollen nerve root by CT myelography had a positive straight leg raising test at less than 50 degrees on the affected side, whereas no one who had a positive straight leg raising test at greater than 50 degrees showed a swollen root. The presence or absence of edematous nerve roots was confirmed at surgery, which was performed on all patients in the study. Changes in nerve root diameter were evident by using the same radiographic technology at 5 weeks and 6 months postoperatively in 8 of the 16 patients. They postulated that compression of the perineural vessels caused inflammatory changes with congestion and edema. The swollen root then is more easily compressed in the neuroforamen and, therefore, they postulated, causes pain. Surgical decompression of the neuroforamen, along with removal of the offending disk material, may allow this congestion and inflammation to resolve, making the nerve less likely to generate nociceptive signals.

To study the notion that compression does indeed cause edema in spinal nerve roots, Olmarker and colleagues[26] used an inflatable balloon secured in proximity to a nerve root in the porcine cauda equina. They tested several different parameters, including the rate of onset of the pressure (0.1 or 15–20 seconds), the sustained pressure (50 or 200 mm Hg), and the duration (2, 10, and 120 minutes). Edema was documented by the spread of Evans Blue–labeled albumin, which is a marker of microvascular permeability. The appropriate investigation of the methodology was done before the study, and sham experiments resulted in negative findings with regard to edema.

In the series that experienced the rapid onset of compressive forces, there was more pronounced edema at 10 and 120 minutes for either pressure than was evident after 2 minutes at either pressure. Therefore, it appeared that with rapid onset of compression, the duration of insult was of more importance in the formation of intraneural edema than was the actual pressure value.

In the second group, which had the gradual onset of the same pressures for the same durations, edema formation was not as pronounced for each data point. For example, compression for 2 hours at 50 mm Hg caused edema only at the edges of the zone of compression and not at the center. Likewise, the 200 mm Hg pressure for 10 minutes resulted in compression zone edge edema only. The results of the 200 mm Hg for 2 hours were similar in both groups, regardless of the slope of compression onset.

The authors postulated that insults that allow a slightly more gradual time of onset for significant compression provide time for the viscoelastic properties of nerve tissue to distribute forces better and, therefore, result in less damage. Rapid onset of compression would provide the nerve tissue with less opportunity to adapt to shear forces and therefore may cause more disruption and edema. The authors postulate that this could result in an intraneural compartment syndrome that would impair the delivery of nutrients and the export of waste products and might thereby compromise neural function. They further state that because spinal nerve roots are not protected by an epineurium or a mechanically durable perineurium they are more susceptible to this type of injury than a peripheral nerve would be. They conclusively demonstrate that compression of spinal nerve roots can result in intraneural edema. This provides one more piece to the puzzle of why herniated disks can cause radicular pain.

Rydevik et al,[31] studied the endoneural fluid pressure in dorsal root ganglion of rats. They subjected these ganglion to ten repetitive gentle compressions by the use of forceps. The measurements of endoneural fluid pressures were repeated and averaged to obtain a single value for each ganglion tested. Five rats were involved. Pressures were measured at baseline and then an average of 81 minutes after the repetitive compression. The values after compression were approximately threefold the values at baseline. This was statistically significant at a very high level of confidence. Subsequent histologic examination revealed edema formation and hemorrhage within the endoneural space of the dorsal root ganglion. They also postulate that a condition analogous to a compartment syndrome can occur in the dorsal root ganglion after mechanical compression and point out that the position of the dorsal root ganglion puts it at risk for such compression with disk herniation. They further review the concept that compression of a normal peripheral nerve or spinal nerve root is likely to result in negative symptoms, i.e., loss of sensation, altered sensation, or muscle weakness. If, however, tissue is inflamed, even minor mechanical stimuli may lead to the positive symptom of pain. They further point out that the dorsal root ganglion in its normal state "may generate a painful response with mechanical deformation." They conclude by stating that elevation in dorsal root ganglion endoneural fluid pressure may be yet another mechanism for the production of nerve root pain.

In 1973, Marshall and Trethewie[22] reported that an extract of glycoprotein from human nucleus pulposus can, when exposed to a guinea pig jejunum model, cause the release of histamine, edema fluids, protein, and another amine, which they believe to be responsible for the pain of migrainous neuralgia and pancreatitis. They postulated that acute pain associated with disk material prolapse is due to local irritation of the nerve root producing edema and the release of protein and "H substances" at the site of injury. They further state that relief by steroids is logical because cortisone inhibits peripheral responses to the H substances. This study was intriguing, yet could be criticized because of the cross-species nature of the model, which may have resulted in positive findings for reasons other than that speculated by the authors.

McCarron et al,[23] in 1987, used homogenized autogenous nucleus pulposus material to inject into the lumbar epidural space of four dogs via an indwelling catheter. The nucleus pulposus material from intervertebral tail vertebrae was harvested after tail amputation and injected into an epidural catheter. Well-developed fibrosis of the dura and the epidural fat were evident. These findings seemed to be quite well defined in distribution.

The authors postulate that annular tears leaking nuclear material may cause inflammatory reactions of the peridural elements and thereby contribute to back pain. Their study indicated that one's own nuclear material could cause this reaction and eliminated the interspecies difficulties with the previous study. They believed that a diskogram showing a relatively normal configuration of contrast that had some evidence of posterior extension of the dye into the neural canal might be the human equivalent of their experimental model. They went on to discuss the surgical implications of this, but did not comment about the role of epidural steroids in these cases.

In 1990, Saal and colleagues[32] published a study that elucidated one aspect of the notion of inflammation of neural elements. They studied phospholipase A_2 activity in disk samples from patients with radiculopathy caused by herniated intervetebral disks. Phospholipase A_2 is the enzyme responsible for liberating arachidonic acid from cell membranes in inflammation. Cyclo-oxygenase then mediates the production of prostaglandins from arachidonic acid while lipoxygenase mediates the ultimate formation of leukotrienes. Therefore, phospholipase A_2 is thought to play a critical role in inflammatory processes.

The authors obtained human intervertebral disk material from five patients who underwent laminectomy with diskectomy. Four had herniated nucleus pulposus causing radiculopathy, while the fifth had degenerative disk protrusions with radiculopathy. Preoperative laboratory and clinical evaluation ruled out collagen and vascular disease or other conditions that might have affected the subsequent experimental results. Clinical and historical evaluation substantiated the diagnosis of radiculopathy. They found that the phospholipase A_2 activity in their extracts was from 20 to 10,000 times higher than phospholipase A_2 activity from any other known human source. Extruded disk and free fragment samples had substantially higher phospholipase A_2 activity than did broad-based herniation samples.

The authors point out the numerous roles in which phospholipase A_2 may mediate inflammatory activity. They cite extensive evidence that suggests that this may be an important aspect of back pain generation in patients who have lumbar disk disease. They further subscribe to the notion that compression alone is probably not the cause of pain in most cases of radiculopathy. They conclude by making the statement that their evidence "suggests that attempts at control of a chemical process by a chemical solution seem more logical than a purely structural approach."

In a guinea pig lung model, Flower & Blackwell[17] studied the effects of steroids on the activity of phospholipase A_2. Their model, which is somewhat complex, involves two isolated perfused guinea pig lungs that are perfused in series. The upstream lung is referred to as the generator and the downstream lung is referred to as the test lung. It is known that thromboxane A_2 release from guinea pig lung is dependent on the activity of phospholipase A_2. Therefore, thromboxane A_2 in the effluent from the downstream (test) lung can provide an indication of phospholipase A_2 activity. When dexamethasone, triamcinolone, or hydrocortisone are perfused directly into the generator lung and the effluent from it is perfused into the test lung, phospholipase A_2 activity in the effluent from the test lung is markedly reduced as measured by thromboxane A_2 release. The authors speculated that the steroid effect involves the biosynthesis of an inhibitory factor and therefore conducted the following experiments:

1. The test lung was pretreated with cyclohexamide, which renders it insensitive to steroid effects by virtue of interfering with both RNA and protein biosynthesis.
2. Steroid was then infused into the preparation upstream of the generator lung.
3. Separately, steroid was infused into the effluent from the generator lung as it was going to the test lung.
4. The effluent from the test lung was then assayed for thromboxane A_2 as a marker of phospholipase A_2 activity.

The results of this second experiment indicated that when steroid was perfused upstream of the test lung, without having gone through the generator lung, that there was no effect on phospholipase A_2 because the test lung had been rendered incapable of synthesizing a steroid-induced inhibitory factor. When, however, the steroid was perfused upstream of the generator lung and that effluent went into the test lung, the phospholipase A_2 activity was markedly decreased. This strongly suggests that the generator lung was capable of synthesizing a steroid-induced inhibitory factor that exerted a direct effect on phospholipase A_2 activity in the test lung and resulted, therefore, in decreased thromboxane A_2 release.

It is thought, then, that steroids exert at least part of their anti-inflammatory action by inducing the biosynthesis of a factor that directly inhibits phospholipase A_2 activity. This would then serve to prevent the release of free fatty acid precursors of prostaglandins and leukotrienes. Since Saal et al demonstrated the extremely high phospholipase A_2 levels in human disk material and the other reports in this section demonstrate incontrovertible evidence of inflammation at the site of disk herniation, it would appear that epidural steroids may exert part of their effect by directly interfering with the ability of phospholipase A_2 to generate chemical inflammatory mediators. One may further speculate that the beneficial effects seen by some investigators of local anesthetic or saline solutions alone, when given epidurally, might be due to irrigating inflamed areas and diluting these mediators. If the supply of substrate for inflammatory mediators was decreasing, as might occur with healing over time, then irrigation and dilution of these mediators could conceivably result in clinical improvement that was temporally associated with an epidural procedure.

COMPLICATIONS FROM EPIDURAL STEROID INJECTIONS

Complications from the techniques reviewed in this article fall into several categories. The most nonspecific category is probably related more to the fact that one is performing an invasive procedure on a patient than it is to the procedure itself.

Symptoms that have been reported in numerous papers included in this article include such things as nausea, mild headaches, dizziness, vasovagal reactions, or related benign transient phenomena, which probably are unrelated to the site or content of injectate.

Several of the authors cited here have reported technical complications that are due to needle placement. Purkis[27] reported two instances of nerve root injury in 58 injections. In one instance the paraesthesia was described as "temporary," however, in the other patient residual numbness in the right C6 dermatome persisted for at least 3 months.

Clearly, the most common technical complication of epidural steroid placement is unintentional puncture of the dura. In the studies cited herein, the incidence of dural puncture ranged from no punctures in 124 injections[34] to 6 of 66 injections (9%),[14] with numerous other authors reporting figures within this range. This complication is thought to be somewhat more likely when one is dealing with operated spines. Waldman[38] reported two dural punctures in a series of 790 cervical epidural steroid injections. Both patients had postural headache symptoms that lasted for over 24 hours and received autologous blood patches (7 mL volume) for treatment of their symptoms. He states that the patients received complete relief of their headaches and went on to resume their series of cervical epidural steroid injections. He makes no mention of any exacerbation of radicular symptoms from the injection of blood, nor does he comment on the exacerbation of compressive symptoms from what amounts to a small iatrogenic cervical epidural hematoma. While unintentional dural puncture is not desirable, unrecognized dural puncture followed by "epidural injection" can be dangerous.

Durocutaneous fistulae have also been reported in conjunction with epidural steroid placements.[2, 15, 21] It is postulated that the deposition of steroids in the needle tract may alter wound healing to the point that the patient is predisposed to form a fistula. The few cases that are reported in the literature are further characterized by repeated needle punctures.

Perhaps the most serious potential complication of epidural steroid therapy is the development of an epidural abscess. Two cases in one report provide a detailed clinical course of epidural abscess following steroid injection.[6] One involved a cervical injection, while the other was done on a lumbar region. Both cases presented 2 to 3 days after injection with complaints of fever and shaking chills. Both patients had temperatures greater than 38.5°C. In the case of the cervical epidural the patient complained of a stiff neck and had meningismus on examination. The patient with the lumbar abscess was a diabetic, and he complained of low back pain and increased sciatica. Both patients developed fairly rapid neurologic compromise and required laminectomy. Laminectomy findings included frank pus in the epidural space. *Staphylococcus aureus* grew from the cultures of both patients.

Waldman[39] reported the development of a subcutaneous abscess at the site of injection in a man treated with cervical epidural steroids. The patient complained of a fever and presented with a "boil" at the injection site. This was treated by superficial incision and drainage and an oral cephalosporin. No sequelae to this were reported.

Two cases of meningitis have also been reported following epidural steroid injection.[15] They both presented with rather fulminant courses and one patient, who also had a durocutaneous fistula, became stuporous and developed multiple severe neurologic deficits. The other patient, despite being quite ill on admission, recovered without residual deficit. Streptococci were isolated in one patient while the CSF report of the other patient simply stated "gram-positive cocci."

Nelson,[25] in 1988, published an alarmist viewpoint of potential complications following intraspinal injections of methylprednisolone acetate. This article reviewed numerous studies that reported complications of this therapy. He highlighted the controversies of both epidural and intrathecal administration of this drug. He focused on the notion that polyethylene glycol, which is contained in methylprednisolone formulations, was responsible for causing aseptic meningitis and other deleterious effects on nervous tissue. He state that methylprednisolone "should not be injected anywhere in the vicinity of neural tissue." He neglected to mention, however, the study published by Benzon et al[4] in 1987, which systematically looked at the effect of polyethylene glycol on neural conduction in a rabbit-sheathed nerve preparation. This study methodically compared different concentrations of polyethylene glycol and analyzed amplitude and conduction velocity changes over exposure times of 1 hour. They were unable to demonstrate any adverse effects of a 3% solution on nerve conduction in sheathed or desheathed nerves. This is the concentration found in commercially available methylprednisolone formulations. As they increased the concentration of the glycol, they found mild-to-moderate depression of compound action potential amplitudes and marked slowing of conduction velocities. The changes they demonstrated were independent of pH and were all reversible after washout. When one considers that the most typical method of injecting methylprednisolone in the epidural space involves the use of saline or lidocaine as a diluent, this concentration is reduced any further. It appears from this study that the neural toxicity of polyethylene glycol in clinically relevant concentrations, is minimal to nonexistent.

Delaney et al[13] examined the effects of epidural triamcinolone diacetate and its vehicle in cats. The animals were killed at 30 and 120 days. Tissue specimens of the level of injection plus one level above and below were examined, including the spinal nerve roots, the root entry zones, and the meninges. Light and electron microscopy was used.

Gross examination showed no abnormalities in any experimental animal at either time of analysis. Microscopic examination revealed minimal meningeal thickening and mononuclear cell infiltrates in an apparent random pattern in control versus experimental group. After 120 days these changes were largely resolved. They concluded that from a meningeal inflammatory standpoint, triamcinolone diacetate injections appeared to be safe.

Several papers have reported on systemic side effects of steroids given by the epidural route. In the first series published in North America, Goebert et al[18] commended that one patient in their group of 113 required treatment for congestive heart failure after epidural steroid injections. They believed that this was secondary to salt and water retention from the steroid. They were using 125 mg of hydrocortisone acetate given three times over 3 to 6 days. Two years later, Sehgal et al[33] reported on assays of steroid presence in plasma and CSF following intrathecal injection of methylprednisolone doses of 80 mg. They found that the steroid persisted in the spinal fluid for approximately 2 weeks after injection. Plasma suppression of cortisol was also demonstrable. Their study was about 3 weeks long, and they noted that, although plasma cortisol levels increased with time after the injection, they rarely returned to baseline levels during the study.

In 1980, Knight and Burnell[20] reported on the development of Cushing's syndrome in four patients following epidural steroid injections. They employed methylprednisolone in doses ranging from 300 to 600 mg over 3 days. These doses are considerably higher than the majority of the literature would suggest is necessary. The authors pointed out that these four cases represented a 2.2% incidence of Cushing's syndrome in 181 injections carried out in a similar manner in their center. They recommended that methylprednisolone be limited to a maximum of 3 mg/kg body weight.

Gorski et al,[19] in 1982, demonstrated that epidural injection of triamcinolone could effectively prevent dogs from increasing plasma cortisol values in response to insulin-induced hypoglycemic stress. This effect lasted 4 weeks after an injection of 2 mg/kg of triamcinolone. They recommended exogenous steroid administration be considered in the perioperative period for patients who have received even a single injection of epidural steroid in the recent past.

In what is perhaps the most comprehensive study of this phenomena, Raff et al[28] demonstrated both acute and chronic suppression of adrenocorticotropic hormone secretion and cortisol levels in patients who had undergone epidural steroid injections with 80 mg of triamcinolone acetate on three separate occasions 1 week apart. They demonstrated a dramatic decrease in adrenocorticotropic hormone at 15 minutes following epidural steroid injection. This effect was present at 1 week after injection. Subsequent epidural steroid injections further suppressed the adrenocorticotropic hormone and plasma cortisol levels. The patients were tested for the ability to secrete cortisol in response to exogenous administration of 250 μg of 1-24 corticotropin, which is a synthetic subunit of adrenocorticotropic hormone. The response to this was subnormal 4 to 5 weeks after the last injection. By 3 months, these parameters had returned to normal. The authors also noted that patients sedated with midazolam had even more pronounced endocrine abnormalities during the study. These patients also recovered from hypothalamic-pituitary-adrenal axis suppression by 3 months.

In light of these findings, it would seem prudent that one of two courses of action be followed when contemplating surgery for a patient who has received epidural steroids in the past several months. The anesthesiologist could empirically elect to treat the patient with steroid coverage during the perioperative period or could obtain plasma cortisol levels at baseline and 1 hour after the administration of 1-24 corticotropin to assess the status of the patients hypothalamic-pituitary-adrenal axis. If the response of this test was normal, no steroid coverage would be indicated.

CONCLUSION

The literature supporting the use of epidural steroid therapy is largely anecdotal and contains very few well-controlled, well-designed studies. Most studies are hampered by employing a multiplicity of diagnostic categories, different sites of injection relative to the presumed level of pathology, different doses of drugs (especially between studies), and clear bias in either the design or the conclusions drawn from the studies.

Despite this, the few controlled studies and the wealth of clinical experience would suggest that there is a role for epidural steroid therapy in the management of certain types of spine-related pain syndromes. Whether epidural steroid injection results are superior to surgical outcome or the natural history of certain conditions is still subject to debate.

Evidence has been reviewed in this article that provides a rational basis for why epidural steroids may be of benefit, based on evidence of inflammation in the pathogenesis of some kinds of degenerative and compressive conditions that give rise to back pain. While rigorous methodologic standards have not been typical in most studies, the wealth of information presented here would suggest that the possibility of efficacy has not been conclusively disproved. Even the harshest critic must admit that "inadequate" proof does not constitute disproof and, therefore, further studies aimed at determining the proper role of steroids given by the epidural route should continue. Future studies should specify diagnostic criteria, use conventionally accepted intervals of both injections and measurements, employ blinding procedures, use placebos that lack the possibility of pharmacologic or physical effects, use realistic follow-up periods, and have significant numbers in each protocol arm to allow clinically relevant and statistically significant conclusions.

Given that the procedures are not entirely free of complications, the learned practitioner, being cognizant of the risks and potential benefits, should help the patient weigh the various factors that influence a decision to receive this type of treatment. The bulk of the papers reviewed herein would suggest that epidural steroid therapy, when applied as one component of a comprehensive approach to the management of chronic and acute pain problems, can, in the hands of the conscientious practitioner, be a useful therapeutic modality.

References

1. Abram SE, Hopwood MB: What factors contribute to outcome with lumbar epidural steroids. *In* Bond MR, Charlton JE, Wolf CJ (eds): Proceedings of the VIth World Congress on Pain, Amsterdam, Elsevier, 1991, pp 491–496
2. Ball CG, D'Alessandro FT, Rosenthal J, et al: Case history number 86: An unusual complication of lumbar puncture: A CSF cutaneous fistula. Anesth Analg 54:691–694, 1975
3. Beliveau P: A comparison between epidural anesthesia with and without corticosteroid in the treatment of sciatica. Rheum Phys Med 11:40–43, 1971
4. Benzon HT, Gissen AJ, Strichartz GR, et al: The effect of polyethylene glycol on mammalian nerve impulses. Anesth Analg 66:553–559, 1987
5. Breivik H, Hesla PE, Molnar I, et al: Treatment of chronic low back pain and sciatica: Comparison of caudal epidural injections of bupivacaine and methylprednisolone with bupivacaine followed by saline. *In* Bonica JJ, Albe-Fessard D (eds): Advances in Pain Research and Therapy, vol I, New York, Raven Press, 1976, pp 927–932
6. Chan S, Leung S: Spinal epidural abscess following steroid injection for sciatica. Spine 14:106–108, 1984
7. Cicala RS, Thoni K, Angel JJ: Long-term results of cervical epidural steroid injections. Clin J Pain 5:143–145, 1989
8. Cohn ML, Huntington CT, Byrd SE, et al: Epidural morphine and methylprednisolone; new therapy for recurrent low back pain. Spine 11:960–963, 1986
9. Coomes EN: A comparison between epidural anesthesia and bed rest in sciatica. Br Med J 1:20–24, 1961
10. Cuckler JM, Bernini PA, Wiesel SW, et al: The use of epidural steroids in the treatment of lumbar radicular pain. J Bone Joint Surg [Am] 67:63–66, 1985
11. Dallas TL, Lin RL, Wu W, et al: Epidural morphine and methylprednisolone for low-back pain. Anesthesiology 67:408–411, 1987
12. Davis R, Emmons SE: Benefits of epidural methylprednisolone in a unilateral lumbar discectomy. Journal of Spinal Disorders 3:299–307, 1990
13. Delaney TJ, Rowlingson JC, Carron H, et al: Epidural steroid effects on nerves and meninges. Anesth Analg 59:610–614, 1980

14. Dilke TFW, Burry HC, Grahame R: Extradural corticosteroid injection in management of lumbar nerve root compression. Br Med J 2:635–637, 1973
15. Dougherty JH, Fraser RAR: Complications following intraspinal injections of steroids; report of two cases. J Neurosurg 48:1023–1025, 1978
16. Evans W: Intrasacral epidural injection in the treatment of sciatica. Lancet 2:1225–1229, 1930
17. Flower RJ, Blackwell GJ: Anti-inflammatory steroids induce biosynthesis of a phospholipase A2 inhibitor which prevents prostaglandin generation. Nature 278:456–459, 1979
18. Goebert HW, Jallo SJ, Gardner WJ, et al: Painful radiculopathy treated with epidural injections of procaine and hydrocortisone acetate: Results in 113 patients. Anesth Analg 40:130–134, 1961
19. Gorski DW, Rao TLK, Glisson SN, et al: Epidural triamcinolone and adrenal response to hypoglycemic stress in dogs. Anesthesiology 57:364–366, 1982
20. Knight CL, Burnell JC: Systemic side-effects of extradural steroids. Anaesthesia 35:593–594, 1980
21. Longmire S, Joyce III TH: Treatment of a duro-cutaneous fistula secondary to attempted epidural anesthesia with an epidural autologous blood patch. Anesthesiology 60:63–64, 1984
22. Marshall LL, Trethewie ER: Chemical irritation of nerve-root in disc prolapse. Lancet 2:320, 1973
23. McCarron RF, Wimpee MW, Hudkins PG, et al: The inflammatory effect of nucleus pulposus; a possible element in the pathogenesis of low-back pain. Spine 12:760–764, 1987
24. Mixter WJ, Barr JS: Rupture of intervertebral disc with involvement of the spinal canal. N Engl J Med 211:210–215, 1934
25. Nelson DA: Dangers from methylprednisolone acetate therapy by intraspinal injection. Arch Neurol 45:804–806, 1988
26. Olmarker K, Rydevik B, Holm S: Edema formation in spinal nerve roots induced by experimental, graded compression. Spine 14:569–573, 1989
27. Purkis IE: Cervical epidural steroids. Pain Clinic 1:3–7, 1986
28. Raff H, Nelson DK, Findling JW, et al: Acute and chronic suppression of ACTH and cortisol after epidural steroid administration in humans [abstract 65]. Program of the 73rd Annual Meeting of The Endocrine Society, Washington, DC, 1991
29. Rocco AG, Frank E, Kaul AF, et al: Epidural steroids, epidural morphine and epidural steroids combined with morphine in the treatment of post-laminectomy syndrome. Pain 36:297–303, 1989
30. Rowlingson JC, Kirschenbaum LP: Epidural analgesic techniques in the management of cervical pain. Anesth Analg 65:938–942, 1986
31. Rydevik BL, Myers RR, Powell HC: Pressure increase in the dorsal root ganglion following mechanical compression; closed compartment syndrome in nerve roots. Spine 14:574–576, 1989
32. Saal JS, Franson RC, Dobrow R, et al: High levels of inflammatory phospholipase A2 activity in lumbar disc herniations. Spine 15:674–678, 1990
33. Sehgal AD, Tweed DC, Gardner WJ, et al: Laboratory studies after intrathecal corticosteroids. Arch Neurol 9:74–78, 1963
34. Shulman M: Treatment of neck pain with cervical epidural steroid injection. Reg Anesth 11:92–94, 1986
35. Swerdlow M, Sayle-Creer W: A study of extradural medication in the relief of the lumbosciatic syndrome. Anaesthesia 25:341–345, 1970
36. Takata K, Inoue S, Takahashi K, et al: Swelling of the cauda equina in patients who have herniation of a lumbar disc; a possible pathogenesis of sciatica. J Bone Joint Surg [Am] 70:361–368, 1988
37. Viner N: Intractable sciatica—The sacral epidural injection—An effective method of giving relief. Can Med Assoc J 15:630–634, 1925
38. Waldman SD: Complications of cervical epidural nerve blocks with steroids: A prospective study of 790 consecutive blocks. Reg Anesth 14:149–151, 1989
39. Waldman SD: Cervical epidural abscess after cervical epidural nerve block with steroids. Anesth Analg 72:717–718, 1991

40. Warfield CA, Biber MP, Crews DA, et al: Epidural steroid injection as a treatment for cervical radiculitis. Clin J Pain 4:201–204, 1988
41. Winnie AP, Hartman JT, Meyers HL, et al: Pain Clinic II: Intradural and extradural corticosteroids for sciatica. Anesth Analg 51:990–1003, 1972
42. Yates DW: A comparison of the types of epidural injection commonly used in the treatment of low back pain and sciatica. Rheum Rehab 17:181–186, 1978

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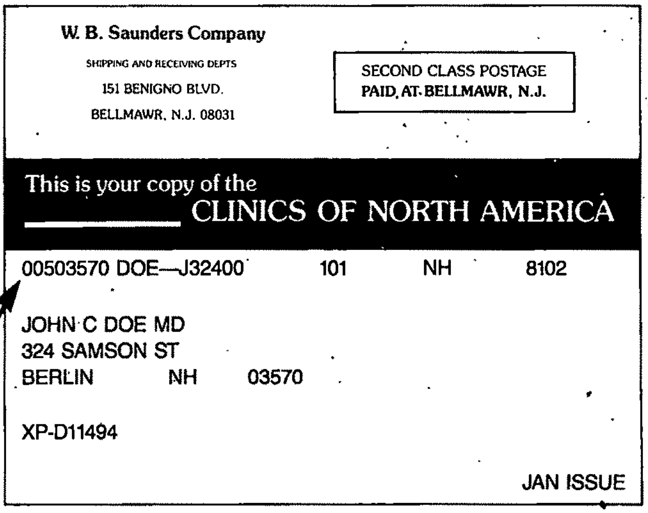

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